A.M.A. Archives OF OPHTHALMOLOGY

SEPTEMBER 1956

VOLUME 56 NUMBER 3

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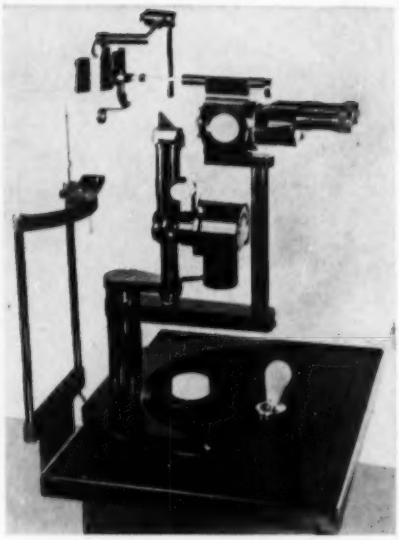

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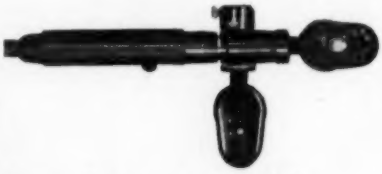

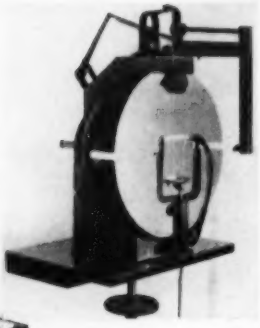

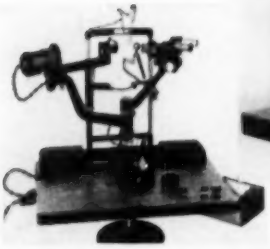

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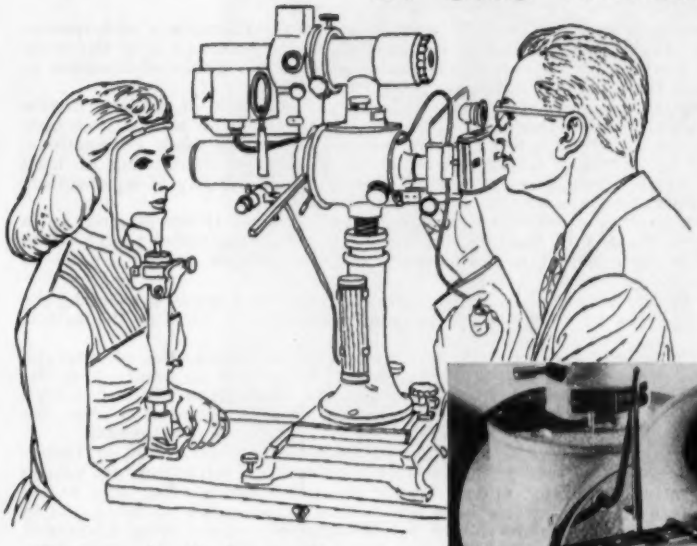

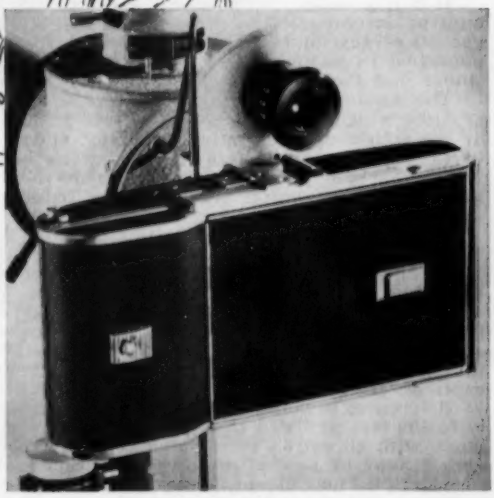

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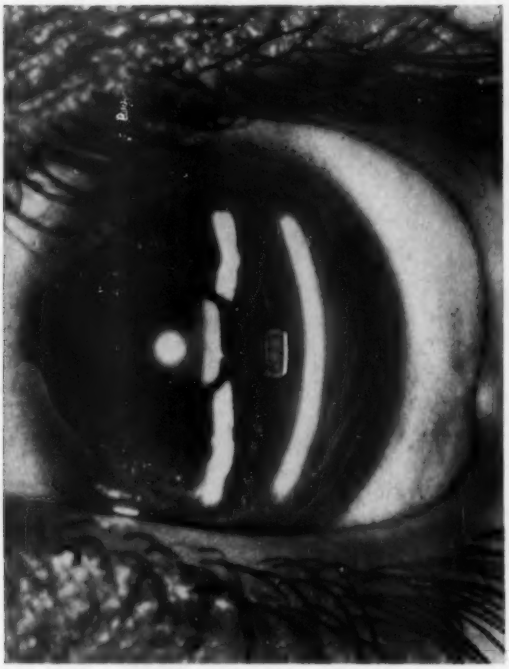

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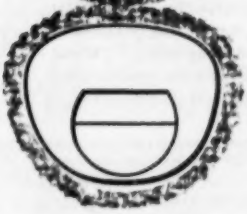

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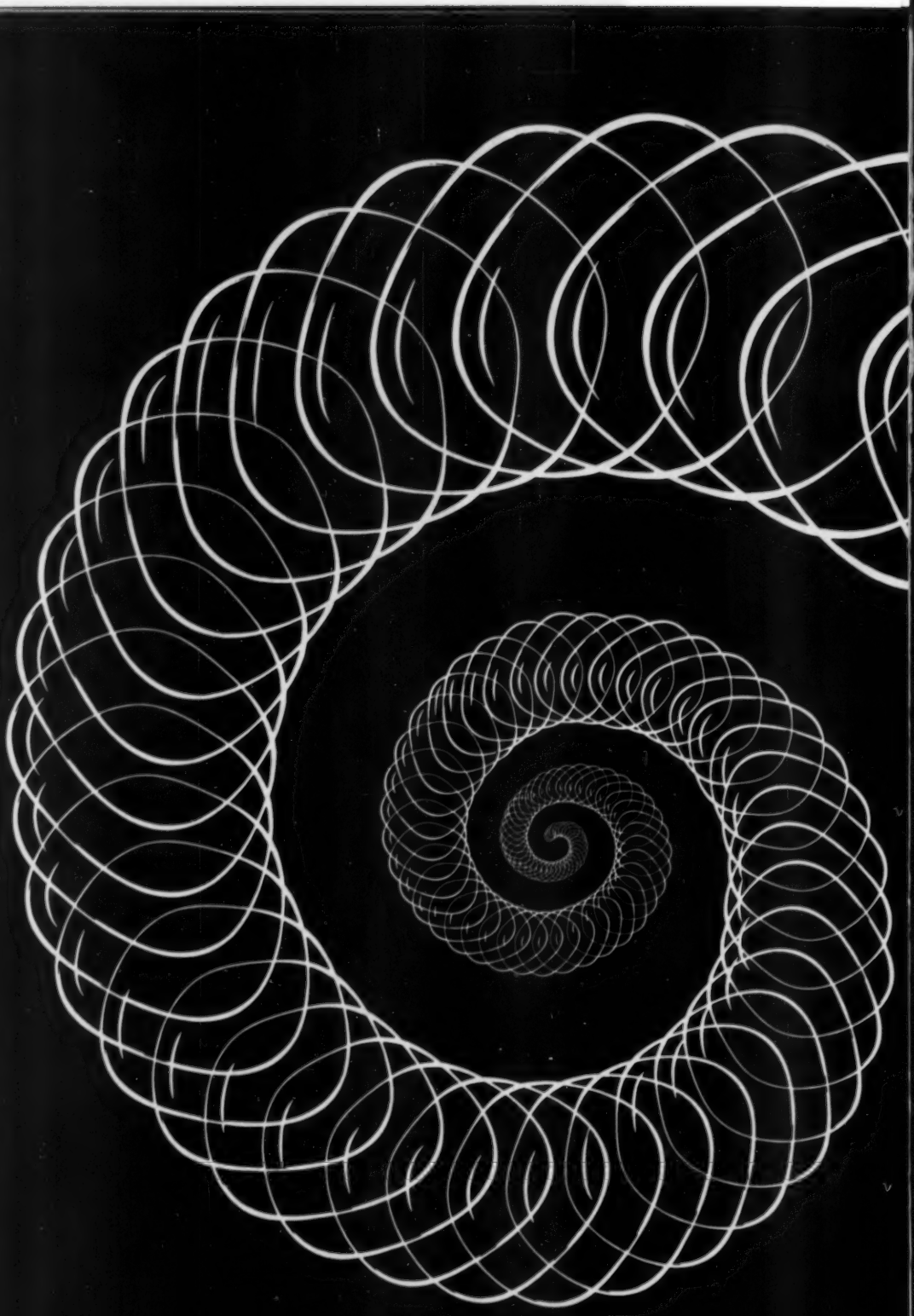

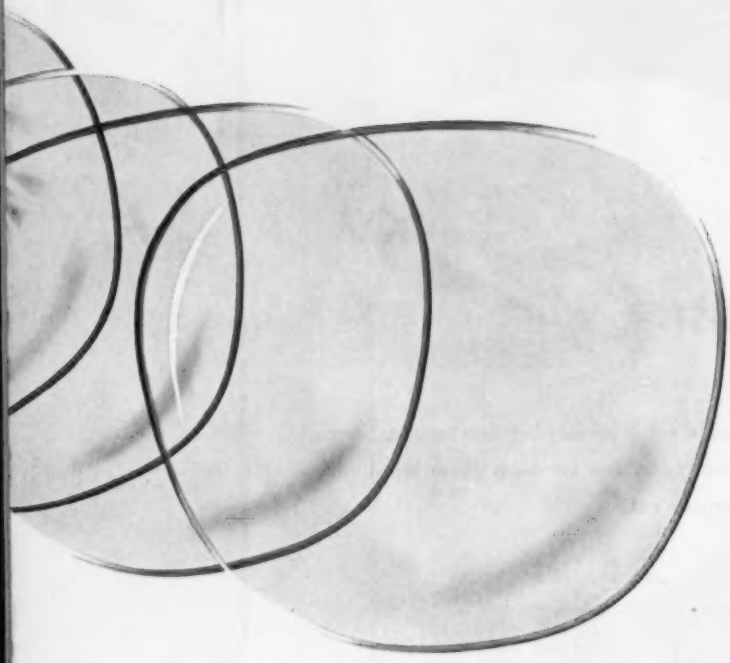

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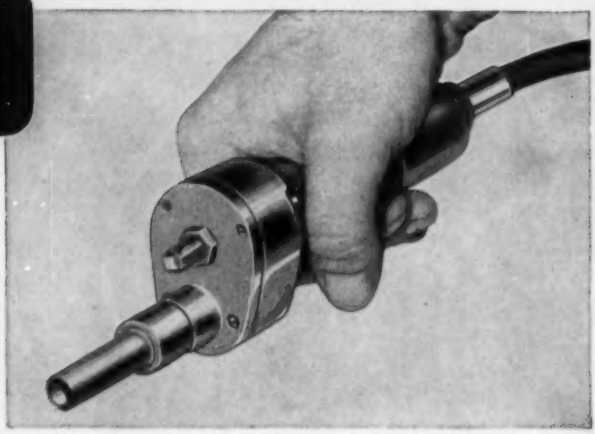

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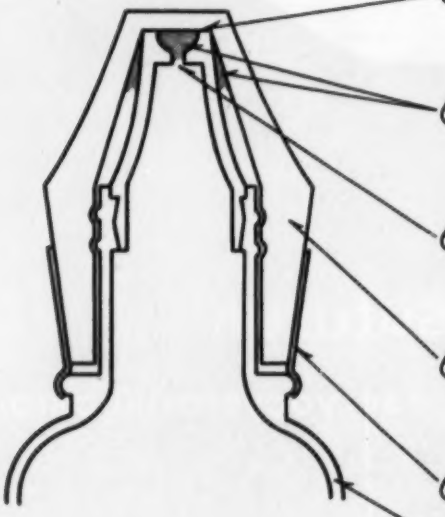

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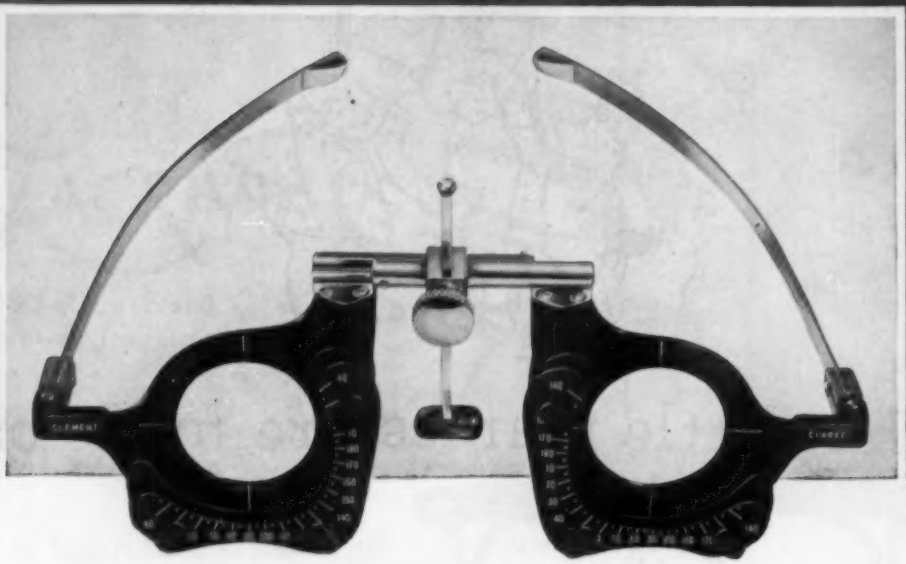

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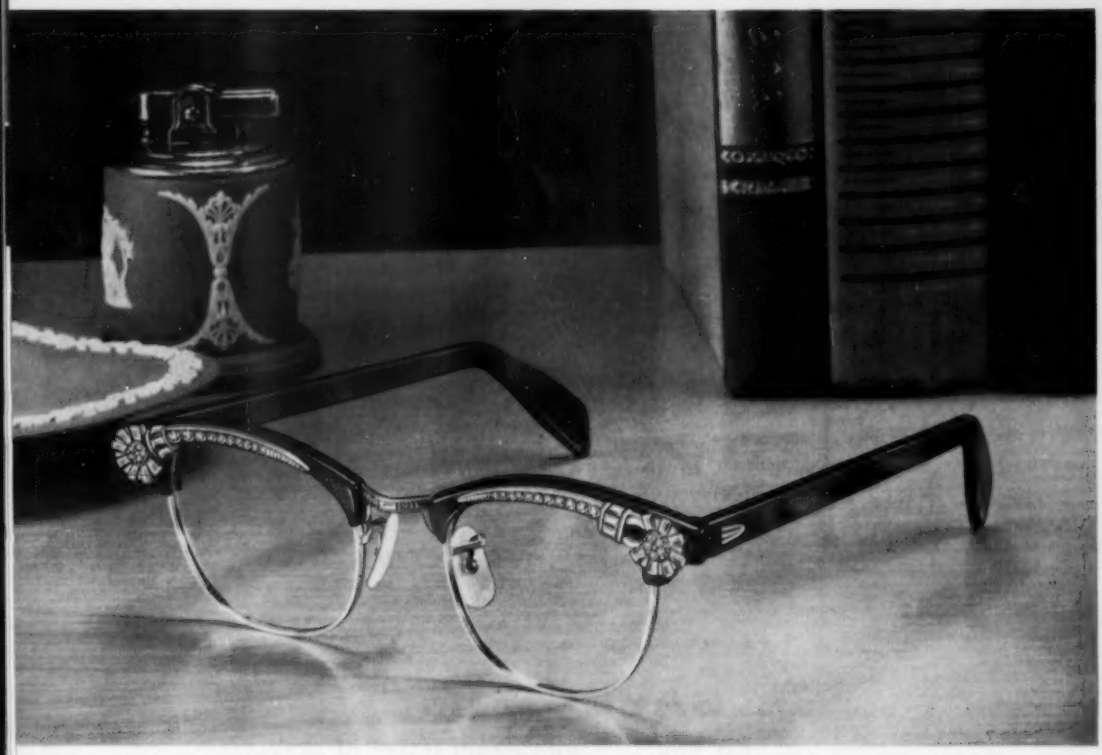

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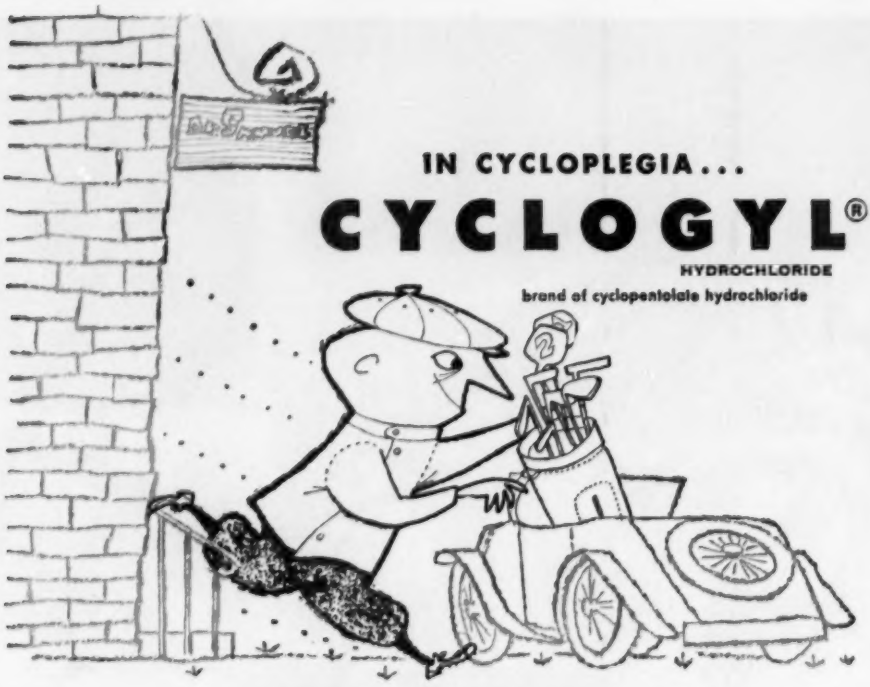

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1. Gordon, D. M., and Ebrenberg, M. H.: Am. J. Ophth. 38:831 *(Dec.) 1954.*

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Water-Drinking and Tonography in the Diagnosis of Glaucoma

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Although characteristic field loss and cupping of the optic nerve head establish a diagnosis of glaucoma, therapeutic efforts in the chronic simple variety of this disease depend upon early detection. Methods available for its diagnosis include tonometry, provocative tests, and tonography.

The use of tonometry in the diagnosis of glaucoma rests upon the fact that elevated intraocular pressure is one of the characteristics of this disease process. Unfortunately, an increase in intraocular pressure has not always been present in all untreated glaucomatous eyes at the time of the examination. Extensive efforts have been devoted to eliciting the pressure elevation. In chronic simple glaucoma the drinking of 1 liter of water has been reported to produce an elevation of intraocular pressure of 8 mm. Hg or more in 29% of eyes.[1] Thus, this provocative test has permitted the detection of glaucoma in some eyes not diagnosed by tonometry alone, but, unfortunately, in only a relatively small number of such eyes.

The estimation of the facility of outflow by such methods as tonography reveals impairment of outflow as a characteristic of most glaucomas.[2] The fact that glaucomatous eyes can demonstrate decreased facility of outflow in the absence of elevated intraocular pressure accounts for their earlier recognition by tonography than by tonometry. Such spontaneous or compensatory hyposecretion of aqueous humor occurs frequently in chronic simple glaucoma and can persist for long periods. When tonography was combined with provocative tests, it was noted that some glaucomatous eyes responded with induced impairment of outflow facility in spite of a failure of this procedure to provoke a rise in intraocular pressure.[3] Thus, tonography before and after water-drinking provided a more sensitive method for the detection of glaucoma than did either alone.

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From the Department of Ophthalmology and the Oscar Johnson Institute, Washington University School of Medicine.

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Unfortunately, most studies of the reliability of these methods have not used independent criteria exclusively for establishing the diagnosis. Thus, many series of glaucomatous eyes reported in the literature have been prejudiced by the inclusion of patients diagnosed on the basis of tonometry, tonography, or a positive water test. If such methods have been used for the selection of the normal and glaucoma groups, it becomes almost impossible to draw valid conclusions as to the value of these tests. For purposes of this report, only those patients were selected in whom the diagnosis of chronic simple glaucoma could be proved by characteristic visual field loss. All 188 eyes so chosen had open angles, had not been operated on, and showed no signs of inflammation or other ocular disease. A similar group of 175 normal eyes were selected from volunteer and clinic patients, with careful avoidance of glaucoma suspects or subjects with ocular defects other than refractive errors. Comparison of these two groups of patients permitted an objective evaluation of the merits of tonography, tonometry, and water-drinking separately or in combination for the differentiation of eyes of the two categories.

Methods and Materials

Tonography was performed with an electronic tonometer before and one hour after the consumption of 1 liter of water. All tests were performed after a 9- to 12-hour fast and without medication for at least three days. The population of 175 normal eyes was accumulated from volunteer hospital personnel as well as eye clinic patients with refraction problems. The 188 glaucomatous eyes were selected so as to include only those eyes which demonstrated characteristic field loss, open angles, and no signs of inflammation and had not been subjected to surgery. Eleven eyes with hypersecretion glaucoma and characteristic field loss were included in the glaucoma group. A larger series of glaucoma suspects and patients with glaucoma but no field loss are under study, but they are not included in this report. Only smooth tonographic tracings were used in this study, and corrections were applied for abnormalities of scleral rigidity and for the increase in episcleral venous pressure during tonography. All interpretations were based on the 1955 tables of Friedenwald.[4] It should be noted that values for facility of outflow so calculated are some 30% higher than previously reported. However, these newer values provide much better agreement with perfusion estimates of outflow facility on the same eye.[5]

Results

Tonometry.—Routine tonometry readings before water-drinking revealed an intraocular pressure of 24 mm. Hg or higher (1955 tables of Friedenwald) in 73 (39%) of the 188 glaucomatous eyes. None of the normal eyes had tonometric readings at this level, because of the method of selection of the normal population. However, it is apparent that pressure alone is a poor criterion for the detection of glaucoma in proved cases.

The Water-Drinking Provocative Test.—One hour after the consumption of 1 liter of water, 53 eyes (28%) of the glaucoma series had a rise in intraocular pressure of 8 mm. Hg or more; none of the normal series sustained such a rise. This was in excellent agreement with the observations of Leydhecker,[1] who found a comparable rise in intraocular pressure in 29% of eyes with chronic simple glaucoma. If less rigid criteria are accepted for positive water-drinking tests, such as a rise of 6 mm. Hg or more, then 78 eyes (42%) of the glaucoma

population would be classified as demonstrating a positive provocative test. However, under these circumstances four (2%) of the normal eyes revealed a similar rise. More significantly, after water-drinking 116 (62%) of the glaucoma eyes had a pressure of 24 mm. Hg or more, whereas in none of the normal eyes did the pressure rise to this level. Thus, the water-drinking provocative test proved of considerable aid in confirming the diagnosis in eyes with established glaucoma. However, the conventional criteria for a positive test failed to detect a very large number of eyes with proved glaucoma.

Tonography.—The distributions of facility of outflow in 175 normal eyes and 188 glaucomatous eyes are presented in Figure 1. The mean value for outflow

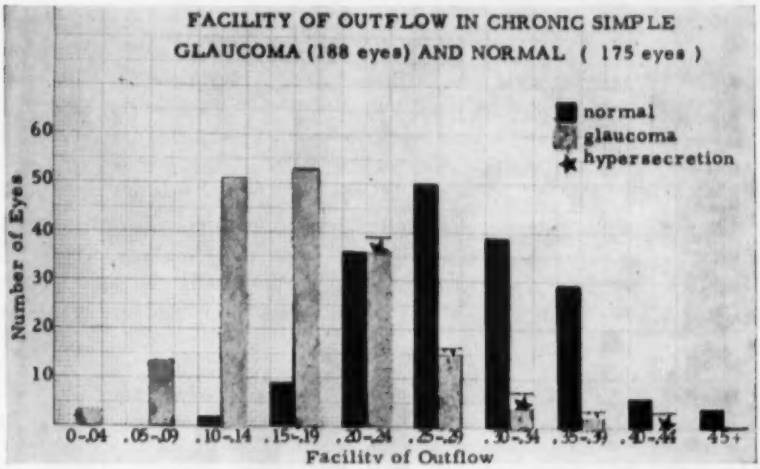

Fig. 1.—Comparison of the distribution of facility of outflow in 175 normal eyes and 188 eyes with chronic simple glaucoma and visual field loss.

facility before water-drinking in normal eyes in this series was 0.31 and for the glaucoma population 0.17 (0.16 without the hypersecretion group). It is apparent from Figure 1 that the two groups of eyes tended to differ as to outflow facility. Unfortunately, a disturbing overlap of facility values occurred in the two groups. Thus, 120 eyes (64%) of the glaucoma series had a facility less than 0.20, but 11 (6%) of the normal eyes fell into this category. Only 2 (1%) of the normal eyes presented a facility less than 0.15, but this criterion reduced the number of glaucoma eyes that could be so diagnosed to 67 (36%). This overlap of glaucoma and normal values was very similar to that described repeatedly in the tonography literature.

Water-Drinking and Outflow Facility.—The effects of water-drinking on the outflow facility are plotted for the glaucoma population in Figure 2 and for the normal population in Figure 3. It is apparent that water-drinking tended to decrease facility values in glaucoma eyes but had less effect on facility of outflow in normal eyes. In fact, the facility of outflow was reduced significantly (10% or more) in 153 (82%) of the glaucoma eyes and in only 32 (18%) of normal eyes. Thus, mean values for facility after water-drinking in normal eyes remained at 0.31 but in the glaucoma series fell to 0.12 (0.11, omitting hypersecretors). Thus, the overlap of facility values between the two populations decreased in magnitude so that 169 (90%) of the glaucomatous and only 8 (5%)

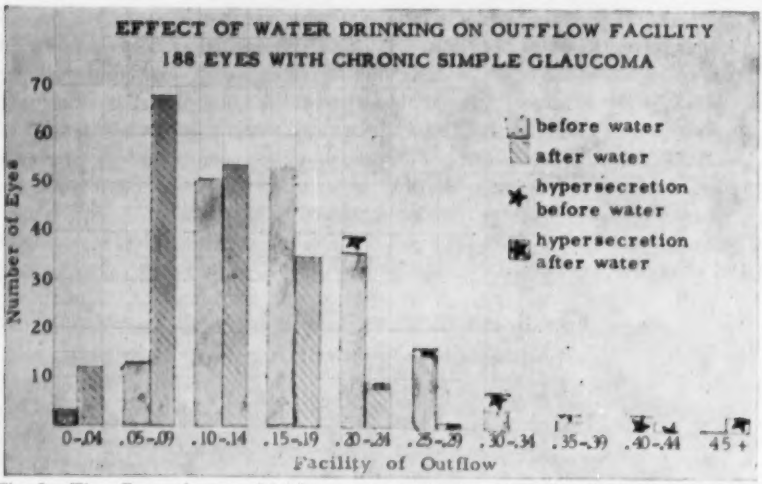

Fig. 2.—The effects of water-drinking on the distribution of outflow facility in 188 glaucomatous eyes.

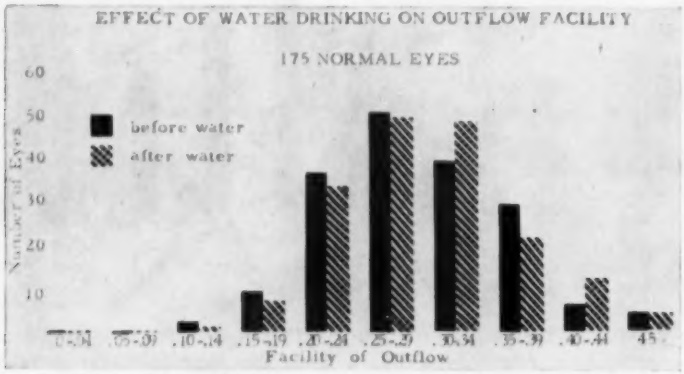

Fig. 3.—The effects of water-drinking on the distribution of outflow facility in 175 normal eyes.

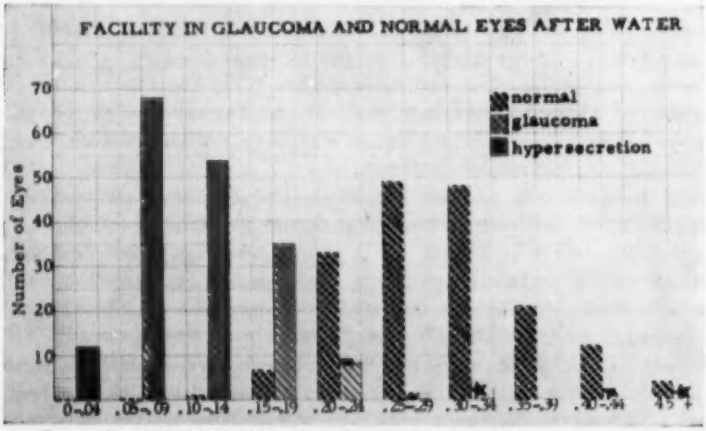

Fig. 4.—Comparison of distribution of outflow facility values in glaucomatous and normal eyes following water-drinking.

of the normal eyes had values for facility less than 0.20. In Figure 4 a comparison of the distribution of facility values in glaucomatous and normal eyes following water-drinking is presented in graphic form.

The Ratio P_0/C.—Since glaucomatous eyes differ from the normal with regard to elevated intraocular pressure (P_0) and decreased facility of outflow (C), both alterations can be included in some simple function, such as P_0/C.* This empirical ratio takes into account both characteristics of glaucoma and so tends to separate the two populations more precisely than does either factor alone. Using the newer tables of Friedenwald and correcting for the increase in episcleral venous pressure, we found P_0/C to be 100 or higher in 133 eyes (71%) of the glaucoma series and in only 3 eyes (2%) of the normals. Since it has been demonstrated that water-drinking tends to produce rises in intraocular pressure and decreases in facility of outflow in glaucomatous eyes and not in normal eyes, the ratio P_0/C is markedly affected in the former group by this provocative test. Thus, after 1 liter of water, 182 eyes (97%) with established glaucoma had values for P_0/C of 100 or more and only 2 eyes (1%) of the normal population fell into this category. Furthermore, all six of the glaucomatous eyes that had failed to respond in this fashion were hypersecretors. Thus, the ratio P_0/C, especially after water, provided one of the best methods of separating the two groups of patients under consideration. A comparison of all of the above methods applied to the data of the two groups of eyes is summarized in the Table.

Comparison of Methods for the Diagnosis of Glaucoma

Method	Normal* (175 Eyes)	Glaucoma* (188 Eyes)
$P_0 \geq 24$	0 (0)	73 (39)
8 mm.Hg+after water	0 (0)	53 (28)
6 mm.Hg+after water	4 (2)	78 (42)
$P_0 \geq 24$ after water	0 (0)	116 (62)
$C < 0.20$	11 (6)	120 (64)
$C < 0.15$	2 (1)	67 (36)
$C < 0.20$ after water	8 (5)	169 (90)
$C < 0.15$ after water	1 (0.6)	134 (71)
10% or more decrease C after water	32 (18)	153 (82)
$P_0/C \geq 100$	3 (2)	133 (71)
$P_0/C \geq 100$ after water	2 (1)	182 (97)

*Percentages are given in parentheses.

Hypersecretion glaucoma is a rare group of the chronic simple open angle glaucomas. It fails to be differentiated readily from normal eyes on the one hand and glaucomatous eyes on the other. Eyes with hypersecretion glaucoma demonstrate elevated intraocular pressure, but in the absence of impaired outflow facility. Most significantly, they lose visual field.[6] The results of tonography and water-drinking in 11 of such eyes with field loss were included with the glaucoma group in Figures 1, 2, and 4 and in the Table. It is of interest that four (36%) of these eyes had intraocular pressure rises of 8 mm. Hg or more after 1 liter of water was drunk. Although tonographic tracings were essential for making the diagnosis of hypersecretion, the disease obviously could not be diagnosed from facility values alone. The distribution of facility values in a

* Several functions can be devised to express this relationship, the simplest of which are C/P_0 and P_0/C. P_0/C has been used in this paper so as to conform with the independent observations of Leydhecker (Leydhecker, W.: Personal communication to the authors).

larger series of such eyes did not differ significantly from the normal. In fact, the hypersecretion group provided an important part of the overlap of outflow facilities in the present study. In this group of 11 eyes, a value for P_0/C of 100 or more was apparent in only two eyes (18%) before and five eyes (45%) after water. However, since hypersecretion glaucoma accounted for only 6% of the glaucomatous eyes in this series and for less than 2% of glaucoma in large clinic populations, these findings should not alter significantly the value of the interpretation of the ratio P_0/C given above. Seven of the eleven eyes with hypersecretion glaucoma had an intraocular pressure of 24 mm. Hg or higher before water, and ten eyes (91%) rose to such a level after water. Thus, intraocular pressure, especially after water-drinking, proved to be the most reliable single criterion for making the diagnosis in this group of cases.

The P_0/C method of interpreting the data can be utilized to separate any group of glaucoma suspects. Based upon the excellent separation of the two groups of carefully selected patients described above, the method has been applied to all patients referred to the tonography laboratory during the past year. It has appeared to be a most reliable and accurate method for the early detection of glaucoma.[7] However, considerable time must elapse before independent criteria of glaucoma diagnosis (e. g., visual field loss) can be utilized to establish definitive correlations in these patients.

Summary

A comparison is presented of tonometry, water-drinking, and tonography on 175 normal and 188 eyes with chronic simple (open angle) glaucoma and loss of visual field. The two groups of eyes could best be separated on the basis of data obtained from tonographic tracings one hour after drinking 1 liter of water. After water the empirical ratio of intraocular pressure to outflow facility (P_0/C) was equal to 100 or more in 97% of this glaucoma series and in only 1% of the normal eyes.

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Unilateral Internuclear Ophthalmoplegia of Vascular Origin

A Report of Four Cases

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Internuclear ophthalmoplegia is an entity arising from lesions of the medial longitudinal fasciculus. The term was first introduced in 1922 by Lhermitte,* and shortly thereafter the condition was divided by Lutz † into the anterior and posterior types. It has been described as a characteristic clinical picture, manifested primarily by paresis of the medial rectus muscle on attempted lateral gaze, other signs of a paralysis of the third cranial nerve being absent. Associated findings of nystagmus, skew deviation, vertigo, nausea, and vomiting have been described.[3]

The medial longitudinal fasciculus is the important reflex pathway connecting the vestibular nuclei to the motor nuclei of the extraocular muscles and of the head and neck. Phylogenetically, it is one of the first tracts of the brain to appear, being present in the Cyclostomata and observed to be an important reflex pathway in fishes.[4] In mammalian embryos it is among the first tracts to be myelinated and maintains a constant location in the vertebrate series. Moreover, its connections with the motor nuclei are unvarying. The vestibular nuclei present a variety of connections to the medial longitudinal fasciculus, the medial nucleus sending ascending and descending fibers to the opposite bundle, the superior nucleus sending ascending fibers to the homolateral fasciculus, and the spinal nucleus giving off descending fibers bilaterally. The medial longitudinal fasciculi receive no fibers from the lateral vestibular nuclei.

The mesencephalic portion of the medial longitudinal fasciculus includes connections to the third and fourth cranial nerve nuclei. The performance of lateral conjugate gaze implies nervous impulses both to the homolateral sixth nerve nucleus in the pontine region and to the contralateral medial rectus center of the third nerve nucleus in the midbrain region. The question of the location of the cross-over site in the medial longitudinal fasciculus remains unsettled. Attempts to produce unilateral lesions experimentally which would aid in localization have been unsuccessful, owing to the close proximity of the two posterior longitudinal bundles.[5] These same studies, however, were able to reproduce the clinical features of bilateral internuclear ophthalmoplegia in the experimental animals.

As judged by the generous clinical and physiologic evidence, the subcortical

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From the Department of Ophthalmology, Division of Surgery, Stanford University School of Medicine, and the Veterans Administration Hospital.

* Reference 1, cited by Duke-Elder [2] and Madonick.[11]

† Reference 2, cited by Duke-Elder [2] and Madonick.[11]

control of lateral conjugate gaze is contained in the area of the closely neighboring vestibular and sixth cerebral nerve nuclei, although no anatomical center has been clearly demonstrated thus far.[6] The abducens complex has been described[7] as consisting of the larger sixth nerve nucleus proper and of a smaller para-abducens nucleus sending fibers through the homolateral medial longitudinal fasciculus to the oculomotor nuclei. This description would imply that the previously mentioned crossing site of the fibers of the medial longitudinal fasciculus would be close to the third nerve nucleus. That this may not be the situation, however, has been demonstrated by the autopsy report of a case of unilateral internuclear ophthalmoplegia by Cogan and co-workers.[8] Their findings revealed the lesion of the posterior longitudinal bundle to be on the side of the ophthalmoplegia, immediately rostral to the sixth nerve nucleus, indicating that the fibers to the medial rectus had decussated in the medial longitudinal fasciculus at least at this level or below.

That some confusion exists regarding the types of internuclear ophthalmoplegia is apparent from the various definitions present in the literature, several of which are almost directly contradictory. Analysis of early definitions of this condition‡ show them to be elaborations upon the more simplified definitions of the unilateral and bilateral forms of the anterior and posterior internuclear palsies. The most acceptable descriptions, based on available anatomical studies and correlated with known clinical and necropsy observations, are those presented by Cogan.[10] The anterior type, in addition to weakness of the medial rectus muscle in lateral conjugate gaze, is manifested by interference with the convergence ability. The lateral rectus muscle is not involved, and nystagmus, though occasionally present, is not as prominent a feature as in the posterior type. In the latter form, on the other hand, convergence is intact, involvement of the lateral rectus may occur, and nystagmus is a prominent feature. Characteristically, horizontal nystagmus, when present, is more marked in the abducted eye. The finding common to both types is palsy of the medial rectus muscle on lateral conjugate gaze. In the posterior type, however, weakness of the homolateral medial rectus muscle may not be readily apparent, owing to the prominence of the involvement of the contralateral external rectus muscle. This fact may explain some of the varied definitions of the posterior type. It should also be restated that, in the anterior type, there is paresis of the homolateral medial rectus muscle, both on lateral conjugate gaze and in convergence, with absence of other signs of a third nerve palsy. Some authors, however, include integrity of convergence as a feature of the anterior type. The accepted location for convergence in the rostral portion of the brain stem makes it difficult to understand how preservation of the convergence ability should be associated with a lesion of the anterior portion of the fasciculus rather than the posterior.

Owing to the aforementioned discrepancies in definition and also due to the fact that cases of internuclear ophthalmoplegia have been confused in the literature with cases of simple paresis of lateral conjugate gaze, evaluation of the frequency of the condition is difficult. In 1951, Madonick[11] stated that there were no more than 20 cases of "anterior internuclear ophthalmoplegia" in the literature. Since that time, only two isolated case reports have appeared in the literature.§ The bilateral form of internuclear ophthalmoplegia is reported by

‡ References 8 and 9.

§ References 12 and 13.

Cogan [3] as being relatively common and as due usually to disseminated sclerosis, inflammations, or neoplasms. Contrariwise, unilateral internuclear ophthalmoplegia is relatively rare. The largest series, including a necropsy report, has been presented by Cogan and co-workers.[3] Their series consisted of eight patients, and the authors reviewed an additional eight cases in the previous literature believed to be unilateral internuclear ophthalmoplegia. The authors' necropsy report is that of a patient who died of generalized lupus erythematosis. The autopsy findings revealed three vascular lesions (infarcts) in the pons, one of which involved the medial longitudinal fasciculus. The lesion was on the side of the weak medial rectus just rostral to the sixth nucleus, suggesting that the fibers connecting the contralateral abducens with the homolateral medial rectus had already crossed. An additional five cases of the series had clinical evidence of generalized vascular disease, and in all eight cases the sudden onsets of symptoms were suggestive primarily of vascular lesion. Spiller's necropsy report [9] of a case of bilateral internuclear ophthalmoplegia showed softening and destruction of both medial longitudinal fasciculi by vascular lesions. The case of Sahlgren and Hofman-Bang [14] showed similar vascular findings.

The pontine region is sensitive to alterations in its blood supply, which arises from two systems, the carotids and the vertebrals. The pontine vessels have a perpendicular course, are lateralized, and are end-vessels. Recently it has been demonstrated [15] that in senescence many of the small branch vessels of the basilar artery have an insufficient lumen to allow their demonstration by injection, as contrasted to their ready demonstration in youth by the same methods. Hence, the explanation for vascular accidents as the major etiology of cases of unilateral internuclear ophthalmoplegia appears extremely valid. Madonick [11] has shown that internuclear ophthalmoplagia can occur without demonstrable lesions, concluding that the clinical signs may be a result of pressure by space-occupying lesions of the posterior fossa.

Report of Cases

The following four cases are presented as representative of unilateral internuclear ophthalmoplegia; three are of the posterior type, and one is of the anterior type. The presumed cause in all four cases was a vascular lesion, although the etiology in each case was different.

CASE 1.—A 30-year-old Negro man was first seen at the Veterans Hospital, San Francisco, on Aug. 20, 1947, giving a history of having fallen down a flight of stairs and striking the right side of his head 13 days previously. He was not rendered unconscious but had been quite dazed. The following morning, on awakening, he experienced frank diplopia and observed that his right eye turned out. The patient had been hospitalized elsewhere for observation for several days. X-rays of the chest and skull had been taken and were negative.

The visual acuity was 20/20 in each eye. In the primary position there was a right monocular exotropia of 37Δ for distance, which increased to 75Δ on left lateral gaze. The patient was unable to rotate the right eye beyond midline on left lateral gaze. Orthophoria was present on right lateral gaze with full duction of each eye. No nystagmus was observed. Convergence was intact, the near point being 3 cm. The pupils were normal in size and reactions. The fundi were normal.

The patient's diplopia lasted one month and then subsided. Seven months after the original date of trauma the patient exhibited only 1Δ of exophoria for

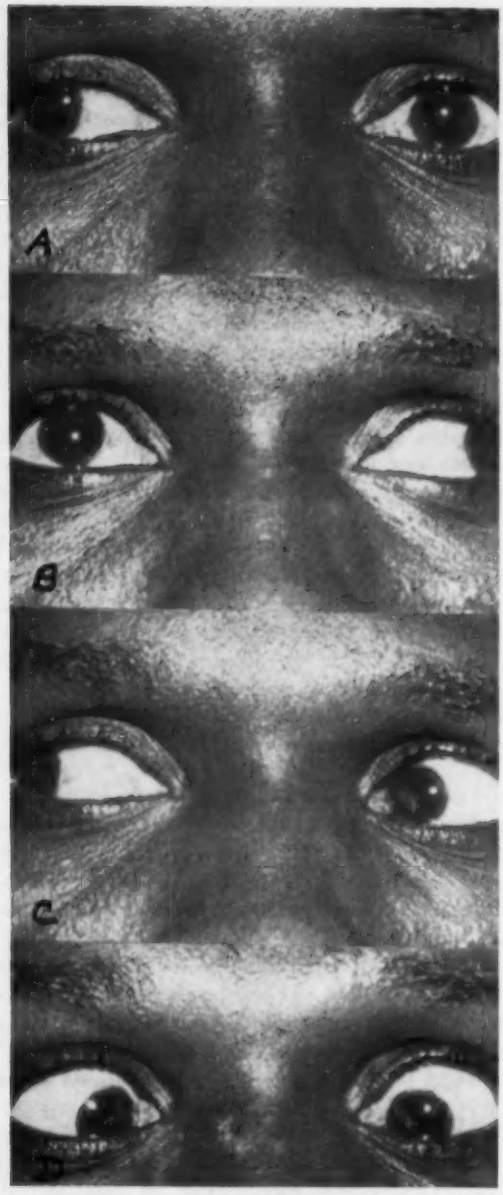

Fig. 1 (Case 1).—*A*, in the primary position of gaze there is right exotropia of 37Δ. *B*, on looking to the left, the right eye does not pass the midline and the exotropia increases to 75Δ. *C*, on looking to the right, there is binocular single vision. *D*, there is normal right internal rectus action in convergence.

distance in the primary position, which increased to 6Δ exophoria on left lateral gaze. End-point nystagmus, which was equal in both right and left lateral gaze, was noted on this examination.

Comment.—This case demonstrated paresis of the right medial rectus muscle only on adduction of the right eye, indicating a lesion of the medial longitudinal fasciculus posteriorly. Convergence was intact, thereby demonstrating the integrity of the convergence center and of the medial rectus portion of the oculomotor nucleus. The palsy was unilateral, the opposite medial rectus muscle performing well in both convergence and adduction of the left eye. The lateral rectus muscles were not involved. The relatively sudden onset of diplopia following trauma and the gradual recovery to normalcy points to a vascular lesion, most likely a small hemorrhage.

CASE 2.—A 63-year-old white man was first examined on Aug. 3, 1955. He gave no history of eye complaint prior to 10 days previously, when, while sitting quietly, he had experienced the sudden onset of diplopia, followed shortly thereafter by dizziness. Both of these symptoms abated slightly, although the patient was annoyed intermittently by a dull headache which had not been present before the episode of diplopia. He was not aware of any alteration of his sensorium, weakness, paralysis, or paresthesias. Several days before hospitalization, he had been told that he had high blood pressure. No symptoms of cardiac decompensation were elicited. Twenty years previously the patient had been treated with arsenicals for latent syphilis.

Initial examination revealed a visual acuity of 20/20 in each eye with correction. There was a left exotropia of 25Δ in the primary position. Full range of motion of both eyes was present on left lateral gaze. There was partial limitation of adduction of the left eye on right lateral gaze. In this direction of gaze, there was a coarse nystagmus of the right eye and a finer nystagmus of the left eye, with the fast component to the right in both eyes. The difference in the amplitude of nystagmus in each eye was readily apparent. The convergence near point was 6 cm. The pupils were normal. The fundi showed only moderate arteriolar sclerotic changes. The patient's blood pressure on entry was 240/120. No cardiac arrhythmias were noted. Blood and cerebrospinal fluid serology was negative.

Twelve days after the initial examination the patient demonstrated 10Δ of exophoria at 20 ft. in the primary direction of gaze. There was an exotropia of 25Δ on right lateral gaze, decreasing to 5Δ of exophoria on left lateral gaze. Subjectively the patient was much improved and did not complain of diplopia except upon extreme right lateral gaze.

Comment.—The signs indicated a paresis of the left medial rectus only on adduction of the left eye. Convergence was intact. These findings denote a lesion posteriorly in the medial longitudinal fasciculus. The right medial rectus was not involved. This case presented an additional feature of nystagmus on right lateral gaze of greater magnitude in the abducted right eye. This finding suggests a slight involvement of the abducens contralateral to the affected medial rectus, and possibly of the vestibular nuclei. The sudden onset of symptoms in the presence of hypertensive vascular disease is suggestive of a vascular lesion, presumably an infarct.

CASE 3.—A 43-year-old white man underwent a right thoractomy and right upper lobe resection for a pulmonary abscess on Feb. 2, 1955. At the time of

Fig. 2 (Case 2).—*A*, in the primary position of gaze there is left exotropia of 25Δ. *B*, on looking to the right, there is weakness of the left internal rectus and horizontal nystagmus, more marked in the right eye. *C*, binocular single vision is present on looking to the left. *D*, the left internal rectus functions normally in convergence.

the freeing of the middle and upper lobes, the patient had a transient episode of hypotension, weak heart action, and very faint peripheral pulses. On several occasions during the operation the diastolic pressure dropped so low that it could not be measured. Vasopressor drugs were utilized during the remainder of the operative procedure, with good response. At the conclusion of the operation difficulty was encountered in re-aeration of the left chest, necessitating bronchoscopy and aspiration of mucus. The patient was ultimately returned to his ward in good condition and with good color. On regaining consciousness the first postoperative day, the patient was aware of diplopia and of a horizontal motion of his environment.

The vision was 20/20 with correction in each eye. There was a left exotropia of 15Δ at 20 ft. in the primary direction of gaze. The exotropia increased to 30Δ at 14 in. Occasionally the patient shifted fixation to the left eye. Initially there appeared to be a weakness of both medial rectus muscles on attempted lateral gaze, but later examinations showed a weakness of only the left medial rectus. Lateral gaze in both directions was associated with marked horizontal nystagmus. On right lateral gaze, nystagmus commenced 20 degrees from the primary position. On left lateral gaze, nystagmus began 1 to 2 degrees from the primary position. The fast components were in the direction of lateral gaze, and the amplitude increased as the limits of gaze were approached. Horizontal nystagmus was also present during upward gaze and on attempted convergence. Convergence was markedly deficient, the near point being 25 to 30 cm.

The neurological examination was negative except for the eyes. An electroencephalogram on Feb. 16 showed abnormality of the right posterior lead. The fundi showed early retinal arteriolar sclerosis. Cerebrospinal fluid examination on the same date revealed a gold curve of 4422110000 and negative serology. Serologic examination of the peripheral blood on admission to the hospital had shown a weakly positive reaction to the VDRL test and a negative reaction to the cardolipin test.

On the date of his last examination, June 1, 1955, the patient demonstrated a constant left exotropia of 10 to 12Δ at distance and of 25Δ at near. The nystagmus was essentially unchanged.

Comment.—This case, as contrasted to the two previous cases, presented a greater variety of signs. The finding of paresis of the left medial rectus muscle, both in adduction of the left eye and in convergence, indicated a lesion of the medial longitudinal fasciculus anteriorly. Again, the lesion was unilateral, since the right medial rectus was spared. Nystagmus was a prominent feature of this case, suggesting involvement of the vestibular nuclei bilaterally and, as stated by Cogan, not necessarily related to the lesion of the medial longitudinal fasciculus. The history of periods of hypotension during surgery is highly suggestive of infarction as the cause of the unilateral internuclear palsy in this case. The possible secondary, additive effects of hypoxia should be considered. The multiplicity of findings could be explained by multiple small infarcts of the brain stem, aggravated by a brief period of hypoxia.

The finding of a paretic type of gold curve in the cerebrospinal fluid also raises the question of an underlying syphilitic vasculitis.

CASE 4.—A 40-year-old white man was admitted to the neurology service of the San Francisco Veterans Administration Hospital on May 8, 1956. Ten days previously, while eating his noon meal, he suddenly had experienced an unusual

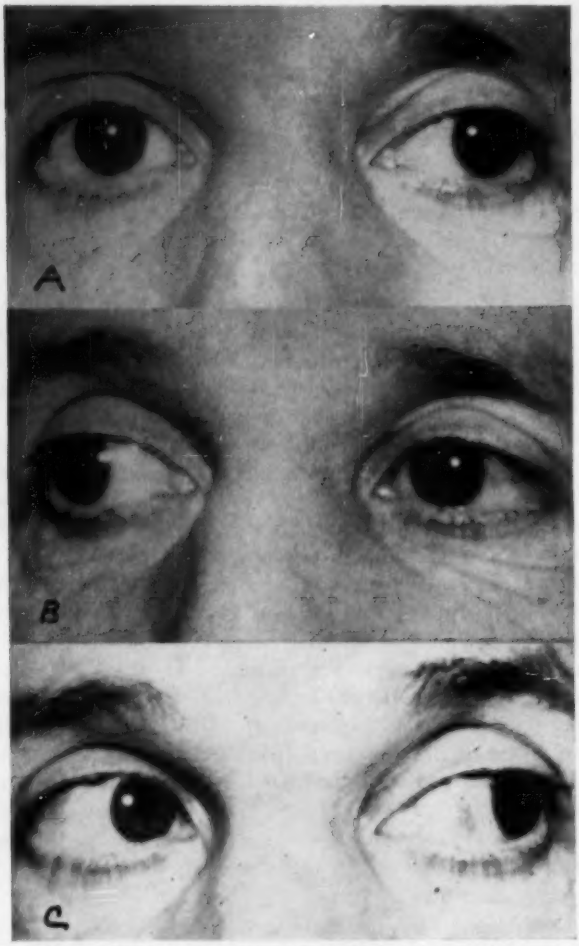

Fig. 3 (Case 3).—*A*, in the primary position of gaze there is left exotropia of 30Δ. *B*, on looking to the right, there is weakness of the left internal rectus and horizontal nystagmus commencing 20 degrees from the primary position. *C*, there is binocular single vision on looking to the left, with horizontal nystagmus commencing 1 to 2 degrees from the primary position. Convergence is absent.

sensation of the left side of his face and difficulty in chewing. One to two hours later, he suffered vertigo, nausea, vomiting, and double vision. He did not note weakness or paralysis of his extremities. The patient was seen by his private physician and was told that he had a left facial paralysis and paralysis of the muscles of the left eye. There was no change in his condition in the week prior to hospitalization.

The patient's past history revealed a diagnosis of rheumatoid arthritis following an episode of low back pain in 1952. Various treatment programs had been instituted, including gold, local and systemic steroids, and phenylbutazone (Butazolidin). The latter drug was given in varying doses continuously from September, 1952, to October, 1954. Three weeks prior to the present illness, the patient again had been placed on phenylbutazone, 100 to 300 mg. daily.

Fig. 4 (Case 4).—*A*, in the primary position of gaze, there is left esotropia of 12Δ. *B*, on looking to the left, there is weakness of the right internal rectus and of the left external rectus. Horizontal nystagmus, more marked in the left eye, is present. *C*, there is binocular single vision on looking to the right, with less marked horizontal nystagmus. *D*, the right internal rectus functions normally in convergence.

Physical examination revealed a blood pressure of 150/105. There was a left facial palsy of the lower motor neuron type. The only other significant physical findings were limited to the eyes.

Visual acuity was 20/20 without correction in each eye. Slight hypesthesia and a mild exposure keratitis of the left cornea were present. The pupils were round, equal, and normal in their reactions. The fundi were normal. A left esotropia of 12Δ for distance in the primary position was present. The esotropia decreased to 8Δ in right lateral gaze and increased to 15Δ in left lateral gaze. Horizontal nystagmus was present in both directions of lateral conjugate gaze, greater in left lateral gaze. In this direction, the amplitude of nystagmus increased as the extreme of gaze was approached and was more marked in the abducted left eye. In left lateral gaze, a readily apparent paresis of the left lateral rectus tended to obscure a weakness of the right medial rectus. The convergence near point was 8 cm.

A lumbar puncture on May 10 disclosed a xanthochromic cerebrospinal fluid, 88 red blood cells per cubic millimeter, and a normal pressure. Serologic tests were negative. The patient's hemoglobin was 17.3 gm. per 100 cc. Hematocrit value was 53%, with slight microcytosis.

Two weeks after hospitalization, esotropia of 6Δ for distance was present in left lateral gaze only. Orthophoria was present in the primary position and in right lateral gaze. Nystagmus was still present in both directions of lateral gaze but of less intensity. The left facial palsy was unchanged.

Comment.—This case demonstrates well how a paresis of the medial rectus muscle may be obscured by a more obvious palsy of the contralateral lateral rectus muscle. The weakness of the right medial rectus was in lateral gaze only, the muscle functioning normally in convergence. These findings point to a posterior lesion of the medial longitudinal fasciculus. The left medial rectus muscle was not involved. Nystagmus, more marked in the abducted left eye, was a prominent feature of this case also. The additional finding of a left peripheral facial palsy suggests a lesion of the left side of the lower pontine region. The findings of xanthochromia of the cerebrospinal fluid, slight elevation of the diastolic blood pressure, and mild polycythemia point to a vascular lesion. Rupture of an aneurysm with subsequent thrombosis of the pontine and arteries can be postulated.

Summary

Four cases of internuclear ophthalmoplegia are presented. Early after its recognition, the condition was divided into the anterior and posterior types. Numerous discrepancies in these definitions, however, have subsequently appeared in the literature. In both types, as implied by the term "internuclear," there is involvement in lateral conjugate gaze of one or both medial rectus muscles. The term "anterior" should be reserved for those cases demonstrating, additionally, interference with convergence of the involved eye. "Posterior" palsies, on the other hand, demonstrate integrity of convergence. In the posterior type, additional findings of sixth nerve involvement and nystagmus are more frequent.

An attempt is made to correlate available clinical and anatomical data with reference to the above definitions.

Four cases of unilateral internuclear ophthalmoplegia are presented. These cases substantiate the suggestion that unilateral forms of internuclear ophthalmoplegia most frequently are due to vascular lesions.

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The Role of the Endothelium in Bullous Keratopathy

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Bullous keratopathy is a state of abnormal corneal epithelial hydration characterized clinically by corneal opacification and the presence of epithelial vacuoles and bullae. In its advanced form, a pannus develops. The stroma becomes vascularized and scarred and, finally, calcium may be deposited in the anterior portions of the stroma. There are probably many factors governing corneal turgescence, and their mechanism is complex. One of the most important factors controlling corneal hydration, and therefore corneal transparency, is the integrity of the corneal endothelium. When this layer is sufficiently damaged, the cornea becomes edematous, and if this edema persists for a sufficient length of time bullous keratopathy develops.

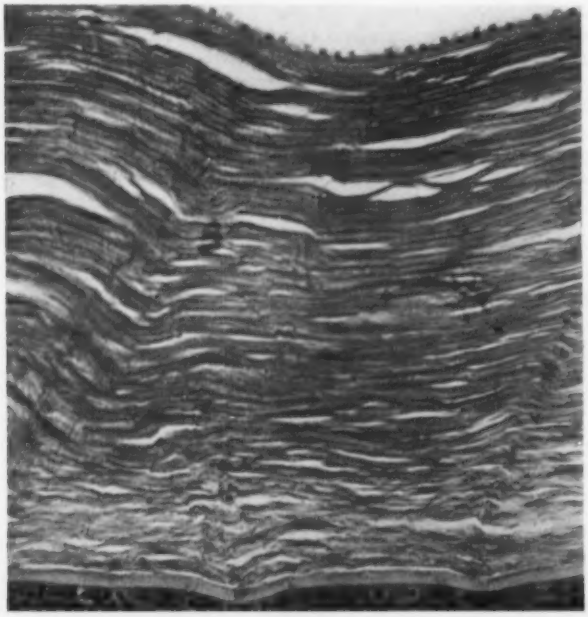

Fig. 1.—Normal cornea in cross section.

The first changes seen in the pathogenesis of bullous keratopathy are in the endothelium. The cells of this layer, which are normally low and rectangular in shape, become flattened and attenuated. Later, their concentration is reduced and finally they may disappear. Figure 1 is a photomicrograph of a normal cornea in cross section, and Figure 2 shows the endothelium of that cornea under

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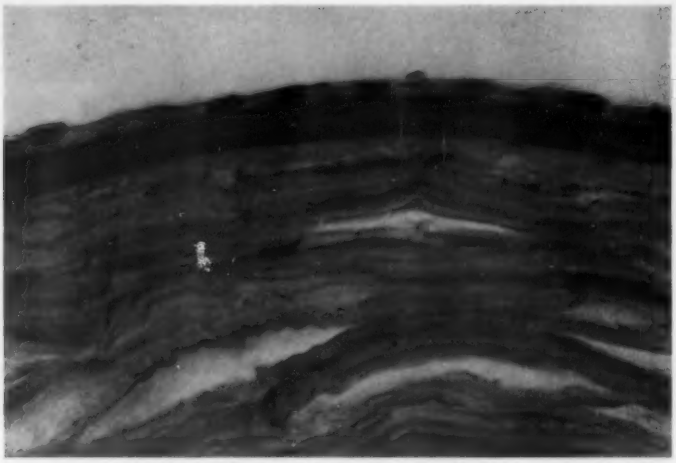

Fig. 2.—Normal endothelium under high power.

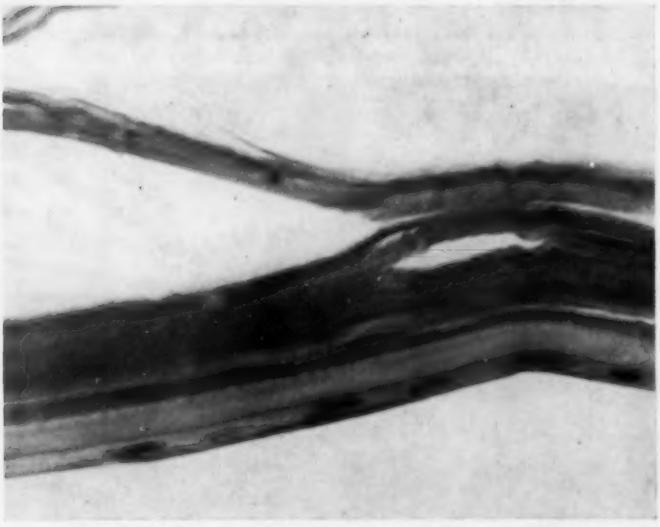

Fig. 3.—Endothelium of cornea with bullous keratopathy.

high power. Figure 3 shows the endothelium of a cornea with bullous keratopathy. Descemet's membrane may develop nodular excrescences between flattened endothelial cells (Fig. 4), or it may become diffusely thickened (Fig. 5). Finally, the stroma shows a diffuse increase in cellularity and a lack of the normal lamellar pattern. It becomes vascularized. A characteristic laminated, comparatively avascular connective tissue is seen between Bowman's membrane and the epithelium (degenerative pannus). The epithelium is irregular in its number of layers; it is edematous, vacuolated, and loosely adherent to the underlying tissue. In such cases the endothelium is always abnormal, and is often absent. Figures 6 and 7 are low- and high-power views of typical bullous keratopathy, illustrating edema of the epithelium, a degenerative pannus, and the altered

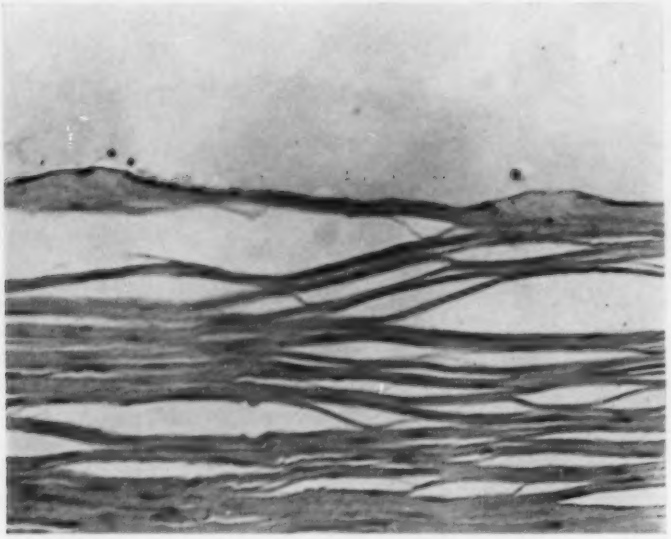

Fig. 4.—Nodular excrescences of Descemet's membrane between endothelial cells.

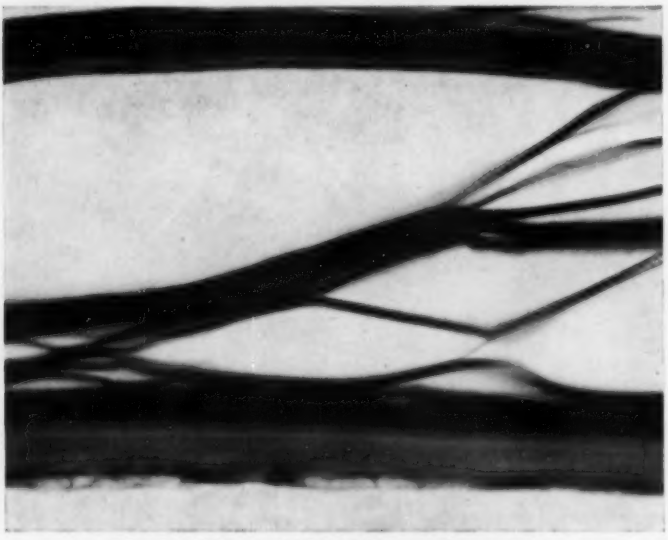

Fig. 5.—Diffusely thickened Descemet's membrane.

endothelium. The deposition of calcium anteriorly is responsible for the appearance of band keratopathy.

Whereas the earliest changes in the endothelium may be difficult to see and evaluate in cross section, they may present strikingly abnormal changes when viewed in flat preparation. Figure 8 is a flat preparation of the endothelium of a normal eye, and Figure 9 is a flat preparation of the endothelium of an eye with bullous keratopathy. The concentration of endothelial cells may be determined with significant accuracy in flat preparation and thereby afford a means

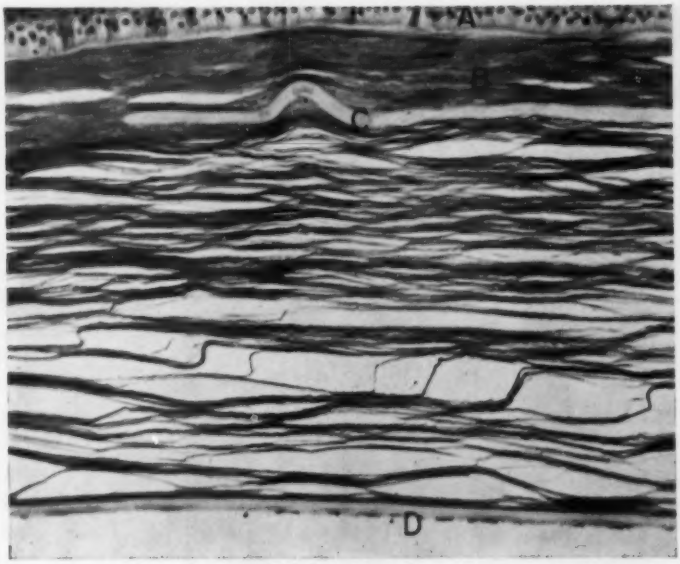

Fig. 6.—Cross section of cornea with bullous keratopathy. *A*, edematous epithelium. *B*, degenerative pannus. *C*, Bowman's membrane. *D*, endothelium.

Fig. 7.—Epithelial edema.

of determining early endothelial damage before the state of persistent abnormal corneal hydration is reached. Studies concerning the variations of normal human corneal endothelium prepared in flat section have been reported in a previous paper.[1] The purpose of this paper is to present additional observations concerning normal corneal endothelium, to discuss the factors leading to a reduction of endothelial cells in pathological corneas, and to correlate these changes with the occurrence of bullous keratopathy.

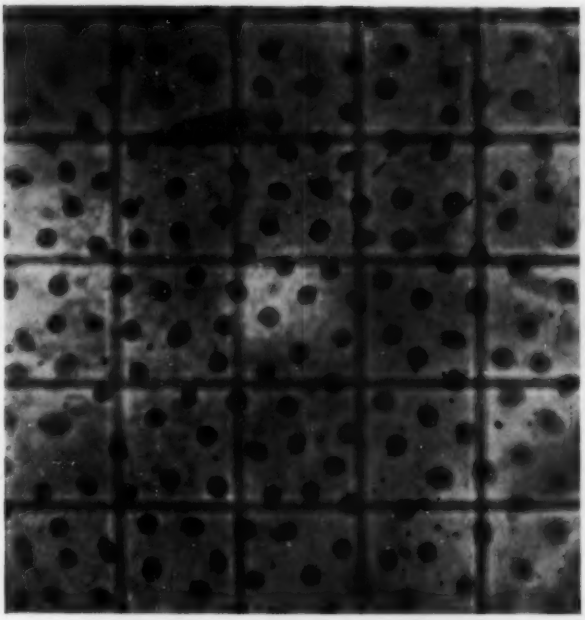

Fig. 8.—Flat section of normal corneal endothelium. (Reproduced from Irvine,[1] *American Journal of Ophthalmology*, Ophthalmic Publishing Company, Chicago.)

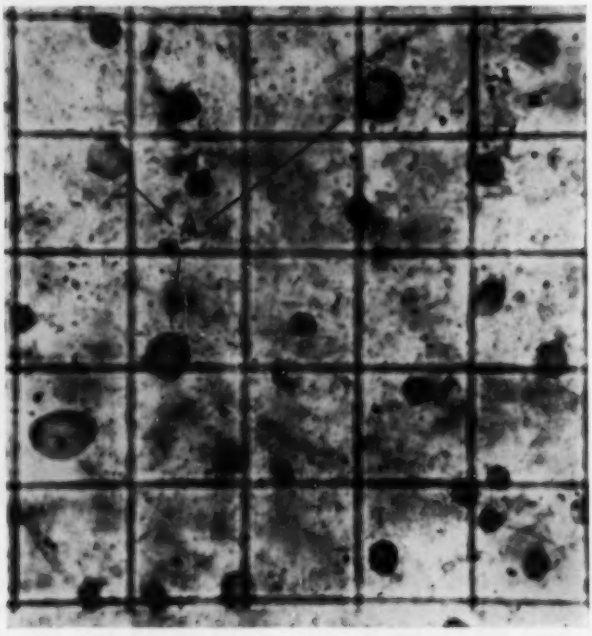

Fig. 9.—Flat section of endothelium of an eye with bullous keratopathy. *A*, endothelial cells.

Previously we determined that the concentration of endothelial cells in a normal cornea is statistically constant but that there is considerable variation of cellular concentration between different normal corneas. From studies of normal eyes removed at autopsy we were unable to explain this variation. We

felt that determinations on normal corneas from enucleated eyes might give more uniform results. Ten such eyes were studied and are reported here.

The variation in the concentration of endothelial cells between the center and the periphery of the cornea was determined in 13 normal eyes from postmortem specimens. Observations were made of pathological eyes having obvious bullous keratopathy, damaged endothelium, or in which there was a clinical history of corneal edema. These will be discussed with reference to the factors that predispose to bullous keratopathy.

The method of preparing flat sections of the cornea and of determining the concentration of endothelial cells has been described previously.[1] The same methods were used in the present study, with the exception that in determining the mean cell concentration of flat sections of the endothelium only 10 fields were counted in each case. In the study concerning the difference between the concentration of endothelial cells centrally and peripherally, 10 fields were picked at random from each of these areas. The extreme periphery corresponding to the area of location of Hassel-Henle warts was excluded. In studying the pathological cases, flat sections were not always made when endothelial abnormality was obvious in cross section, but they were made when the changes were questionable.

Results

Chart 1 summarizes the data concerning the endothelial-cell concentration of

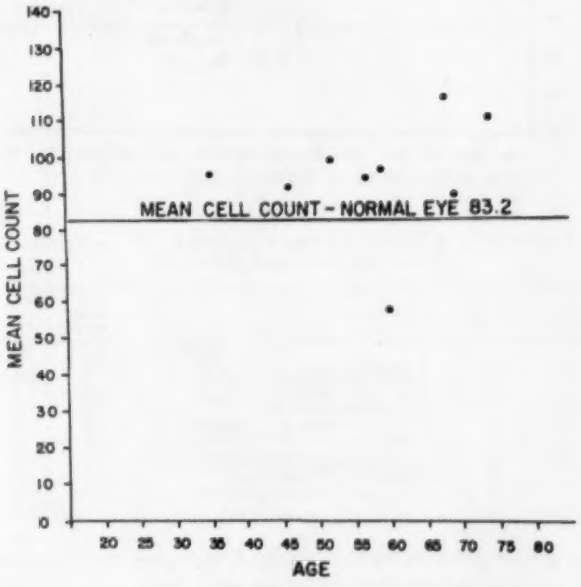

Chart 1

10 normal corneas from eyes enucleated during life. Chart 2 summarizes the data from 64 normal eyes removed at autopsy. Four pathological cases are included for comparison. Table 1 summarizes the data concerning 10 normal eyes enucleated during life. Table 2 summarizes the data concerning the differences in endothelial-cell concentration between the center and the periphery of the cornea.

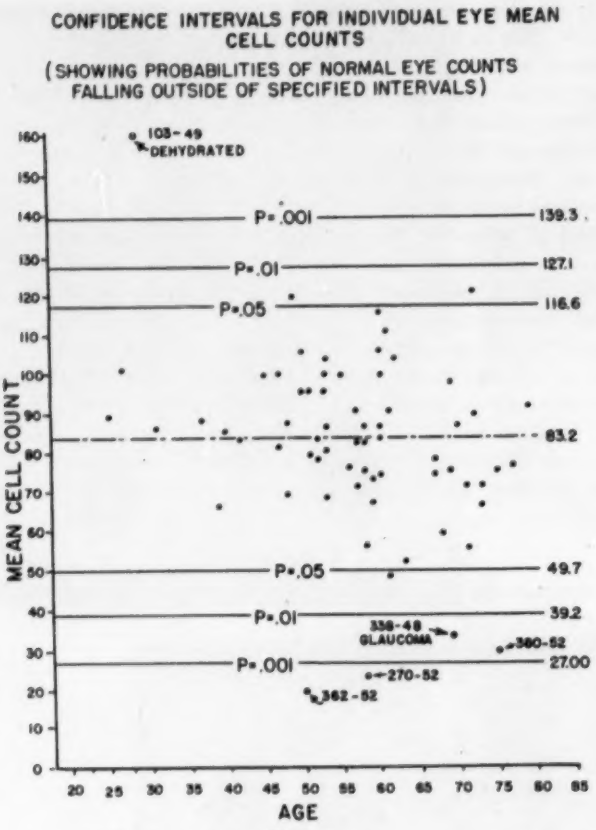

Chart 2

TABLE 1.—*Summary of Data Concerning Flat Sections of Ten Normal Corneas from Eyes Enucleated During Life*

Case	Age, Yr.	Diagnosis	Fields Counted	Mean Cell Count
10	35	Malignant melanoma of choroid	10	96
11	46	Malignant melanoma of choroid	10	92
12	52	Malignant melanoma of choroid	10	100
13	57	Essentially normal eye	10	95
14	59	Malignant melanoma of choroid	10	97
15	59	Malignant melanoma of choroid	10	142
16	68	Malignant melanoma of choroid	10	117
17	69	Malignant melanoma of choroid	10	90
18	60	Neurofibroma of right orbit	10	59
19	74	Malignant melanoma of choroid	10	111

Chart 3 is a graph of these data. Table 3 indicates the commonest factors damaging the corneal endothelium as ascertained from a study of pathological specimens from the Estelle Doheny Eye Foundation.

Comment

The data presented in Charts 1 and 2 indicate that there is considerable variation in the concentration of human corneal endothelial cells. Although the difference is not as great in the eyes enucleated during life as it was in those re-

TABLE 2.—*Concentration of Corneal Endothelial Cells at the Center and at the Periphery of the Cornea*

Case	Age, Yr.	Mean Cell Count per High-Power Field		Difference
		Center	Periphery	
20	53	54	102	48
21	79	74	84	10
22	63	50	56	6
23	52	70	83	13
24	60	87	104	17
25	48	76	86	10
26	48	74	83	9
27	57	60	79	19
28	56	71	83	12
29	53	63	81	18
30	69	73	84	11
31	42	67	81	14
32	51	118	140	22

TABLE 3.—*Histopathological Findings Associated with Bullous Keratopathy in Enucleated Eyes Received at the Estelle Doheny Eye Foundation*

Pathological Findings	Cases, No.
Glaucoma	47
Intraocular inflammation	13
Intraocular hemorrhage	13
Primary endothelial dystrophy	4
Keratoconus	1
Glaucoma, hemorrhage, and inflammation	73
Total	151

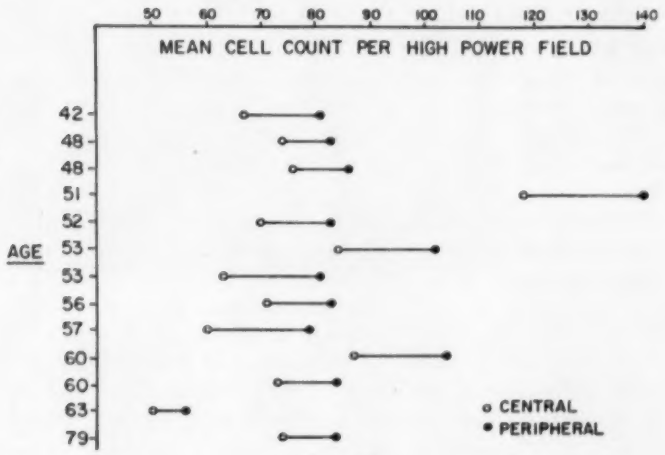

Chart 3

moved at autopsy, it is of sufficient magnitude to be of interest. The normal variation of our findings in the concentration of cells is consistent with clinical observations relating to the difference in onset, duration, and severity of corneal edema in patients having diseases of a similar nature and severity. For example, there may be a difference in degree of corneal edema in patients with iridocyclitis.

One may have marked clouding with a mild form of iritis, and another may have comparatively little edema, although other findings would indicate that the inflammation was severe. Such normal variations in endothelial-cell concentration might affect the levels of intraocular pressure governing the onset of corneal edema. The presence of deterrent factors such as blood in the anterior chamber, intraocular inflammation, adherence of the vitreous to the endothelium, or increased intraocular pressure might well have a severer affect on the normal cornea with the smaller concentration of endothelial cells.

The difference in concentration of endothelial cells between the center and the periphery of the cornea is consistent with the apparent pathological physiology and clinical characteristics of several conditions. The data presented suggest that the concentration of cells is normally approximately 15% less in the center than at the periphery of the cornea (Table 2). This observation is consistent with the clinical experience that bullous keratopathy is first apparent, and is severest in the central portion of the cornea. It is in keeping with the predilection of corneal gutatta to involve the central cornea first, and to a greater degree than the periphery. A gradual uniform depression or degeneration of the endothelium would be expected to cause persistent corneal edema centrally first if there are fewer cells in that area. This seems more logical than to postulate that the endothelium of the central cornea is singularly and peculiarly affected in endothelial dystrophy. The practical application of this observation in corneal grafting operations has been discussed by Stocker[2] in his excellent monograph. He and others stress the use of large grafts in patients with endothelial dystrophy.

In our experience, glaucoma is the commonest cause of endothelial atrophy and degeneration, which if unchecked leads to bullous keratopathy. The gradual diminution of endothelial-cell concentration in cases of chronic glaucoma is consistent with the different levels of tension at which different glaucoma patients develop corneal edema. For example, Case 9 reportedly had a clear cornea with Schiøtz tonometer readings of 60 and had a mean cell concentration of endothelium of 79 cells per high-power field. Case 5 developed corneal edema when the tension rose above 35 units (Schiøtz). The endothelial cells were reduced to 40 cells per high-power field. This low normal count represents a borderline abnormality that may account for the cloudy cornea at relatively low tension levels.

The intraocular pressure at which a cornea becomes abnormally hydrated might be directly related to the duration, and possibly the severity, of the glaucoma. Case 8 is an illustration. When this patient was first seen, he could tell by the presence of halos when his intraocular pressure was above 40 (Schiøtz). Two and a half years later his symptoms would become apparent with tension above 25. The more frequent occurrence of abnormal corneal turgescence in glaucomatous patients after cataract extraction is well known. This may occur even though the surgery is uncomplicated and the tension remains controlled. The trauma of surgery is apparently sufficient to cause a borderline endothelium to undergo further deterioration and be no longer able to support normal stromal hydration. Adhesions of vitreous to the cornea are more prone to cause corneal edema in a glaucomatous patient than they are in a nonglaucomatous patient. A consideration of these factors might induce the surgeon to vary his technique, such as by sliding the lens, by making a more posterior section, or by performing an extracapsular extraction in suitable cases.

Other factors causing endothelial degeneration and predisposing to bullous keratopathy are intraocular inflammation, hyphema, trauma, abiotrophy, and any disease involving the corneal endothelium. These have been discussed in detail by Simpson.[3] I will therefore cite a few cases that illustrate the decrease in concentration of corneal endothelium.

Case 3 is given as an example of the effect of severe and prolonged inflammation on the endothelium. Although the patient did have a secondary glaucoma that subsided after iridectomy and irrigation of cataractous lens remnants from the anterior chamber, the posterior segment was essentially normal. This is strong indication that the glaucoma was mild and insufficient to cause the marked degenerative changes in the endothelium. The cells of that layer were reduced to 23 cells per high-power field (Fig. 10), as compared with the normal concentration, approximately 80 cells per high-power field. The cornea was very

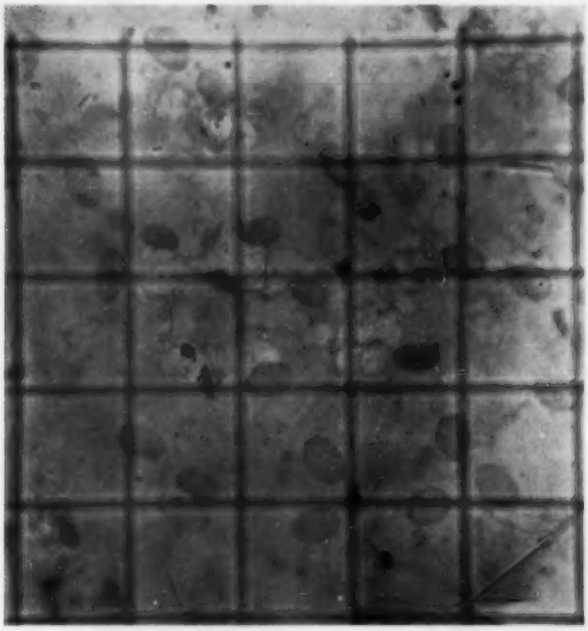

Fig. 10 (Case 3).—Flat section of endothelium showing greatly reduced concentration of cells per grid field.

edematous at the time of enucleation. This case also illustrates the relationship of keratic precipitates to areas of altered endothelium (Fig. 11).

The juxtaposition of vitreous to the endothelium at times causes the overlying stroma to become edematous. This is more likely to occur if there have been other deleterious factors such as glaucoma, inflammation, or primary endothelial dystrophy. Case 4 suggests that bullous keratopathy may occur after cataract surgery in an eye that was clinically normal preoperatively except for the lens changes. There was vitreous in the anterior chamber after surgery. In this elderly patient, nutritional factors such as anemia and/or senescent endothelial changes might have contributed to the onset of irreversible corneal edema.

Whether the presence of free blood in the anterior chamber will cause degeneration of the endothelium is debatable. This condition is so often complicated

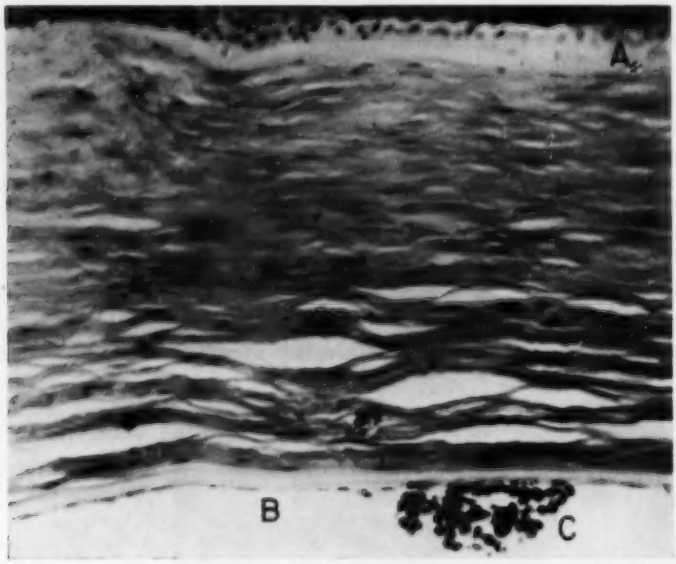

Fig. 11 (Case 3).—Relationship of keratic precipitate to abnormal endothelium and edematous epithelium. *A*, edematous epithelium. *B*, endothelium. *C*, pigmented keratic precipitate.

by glaucoma, trauma associated with surgery, and inflammation that it is difficult to evaluate the affect of the blood alone. Many times the blood may absorb without leaving any trace. It may hemolyze with or without the stimulus of glaucoma. It may organize or cause the formation of a peculiar, typical connective tissue which is thought to arise from metaplasia of the endothelium. In such instances the endothelium is flattened and attenuated and resembles the connective tissue. Case 6 indicates that blood might cause endothelial deterioration without the presence of significant glaucoma. The patient was young; there was

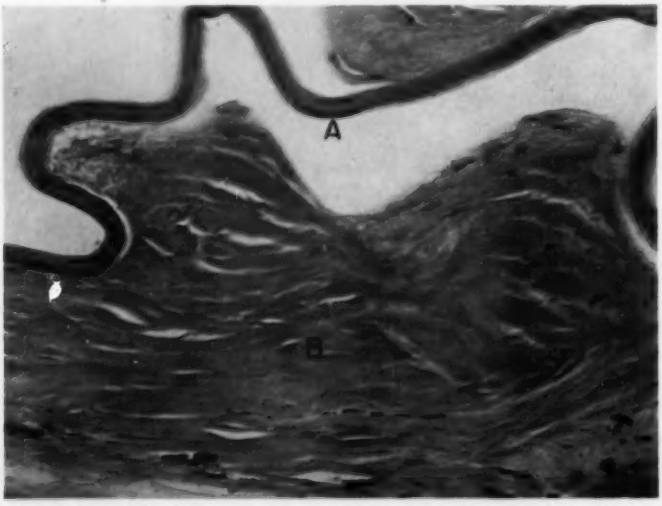

Fig. 12 (Case 7).—Endotheliogenous connective tissue resulting from hemorrhage into the anterior chamber. *A*, Descemet's membrane. *B*, endotheliogenous connective tissue.

no history of previous corneal disorder, and the duration of his illness was only six weeks. Also, there was neither clinical nor pathological evidence of glaucoma. Indeed, the pathology found is usually associated with hypotony. Case 7 is presented to illustrate the endotheliogenous connective tissue that probably represents a response to hyphema (Fig. 12). It is of interest that clinically this resembled an epithelial downgrowth.

Summary

The pathology of bullous keratopathy is initiated by changes in the corneal endothelium that permit the cornea to become abnormally hydrated. These changes are reflected by a decreased concentration of endothelial cells which can be quantitatively studied in flat preparation. The concentration of human corneal endothelium varies between normal persons and between the center and periphery of individual corneas. The possible significance of these normal variations is discussed. Some of the pathological factors causing degeneration and atrophy of the corneal endothelium and predisposing to bullous keratopathy are presented. Abstracts of pertinent and illustrative cases are appended.

Report of Cases

CASE 1.[1]—A 75-year-old man had had a penetrating wound of the ciliary body two months prior to enucleation. He developed a hypermature cataract and glaucoma, and the eye was removed because of "absolute glaucoma."

Histologically the posterior segment was normal, but the corneal endothelium was flattened and attenuated. The mean cell count was reduced to 39 cells per high-power field. The cornea had been edematous clinically, but there was little evidence of edema in the fixed specimen. This is given as an example of early endothelial degeneration secondary to glaucoma.

CASE 2.[1]—A 50-year-old man had chronic open angle glaucoma. The eye was blind. Clinically and pathologically it showed the typical findings of advanced glaucoma and bullous keratopathy. The mean cell count of the corneal endothelium was reduced to 19 cells per high-power field. This is an example of advanced endothelial degeneration secondary to glaucoma.

CASE 3.[1]—A 58-year-old woman developed iridocyclitis and mild secondary glaucoma after extracapsular extraction of a hypermature cataract. The tension was normalized after iridectomy, and the inflammation subsided after cortical material was irrigated from the anterior chamber. The cornea remained cloudy. There were a few cells in the anterior chamber of the other eye, and the first eye was enucleated because of the possibility of sympathetic ophthalmia. The posterior segment was normal.

The corneal endothelial cells were reduced to 23 cells per high-power field. This is an example of the effect of severe and prolonged inflammation on the endothelium.

CASE 4.—A 75-year-old woman had had pernicious anemia for many years. Persistent corneal edema developed after an uncomplicated intracapsular cataract extraction. Vitreous was seen in the anterior chamber in contact with the cornea. The cornea of the other eye was normal. Bullous keratopathy developed. There was no useful vision. Fourteen years after the operation the eye was enucleated because of pain and redness associated with corneal ulceration.

Histologically there was little evidence of glaucoma. Ganglion cells were plentiful, and the nerve was neither atrophied nor pathologically excavated. In

cross section the endothelium was atrophied. An occasional pale-staining large oval nucleus, recognizable as endothelium, could be seen in flat section. Inflammatory cells were seen on the endothelial surface. This case illustrates the endothelial change possibly caused by the apposition of vitreous and the posterior corneal surface.

CASE 5.—A 68-year-old man had an extracapsular cataract extraction 10 years prior to enucleation. The eye had been glaucomatous for three years. The highest tension recorded was 47 units (Schiøtz), and the cornea became edematous if the tension rose above 35 units (Schiøtz).

The endothelial cells were reduced to 40 cells per high-power field. This low normal count may represent a borderline abnormality that explains the cloudy cornea at comparatively low tension levels.

CASE 6.—A 39-year-old white man had had a penetrating injury to the left eye in November, 1950. An intraocular foreign body was removed through the corneal wound of entry. A large iris prolapse was excised, and the cornea was closed. The anterior chamber was filled with blood. Six weeks after the injury the eye had had several recurrent anterior chamber hemorrhages and was still irritable and painful. The intraocular pressure was 16 mm. (Schiøtz). The eye was thought to be blind and was enucleated because of the possibility of there being sympathetic ophthalmia.

Histologically the corneal endothelium was flattened and attenuated and the number of cells was greatly reduced. There was free blood in the anterior chamber, in the vitreous, and beneath the retina. The optic nerve was not obviously atrophied. Ganglion cells were essentially normal for a vertical section, and the nerve fiber layer was neither thinned nor gliosed. This case illustrates the damage to endothelium possibly caused by hyphema.

CASE 7.—A 73-year-old white man had had an extracapsular cataract extraction performed upon his right eye in 1949, after which the cornea gradually became cloudy. When he was first seen by the reporting ophthalmologist, there was a dense membrane in the anterior chamber, along the posterior surface of the cornea and anterior surface of the iris, that suggested the possibility of the presence of an epithelial downgrowth. The tension was elevated to fingers but was not described as hard. The vision was reduced to light perception.

The gross examination indicated that the corneal epithelium was denuded in the upper half. There were broad peripheral anterior synechiae. The anterior chamber was shallow.

Microscopically the cornea was denuded of epithelium over most of its surface. The corneal stroma was diffusely scarred and edematous. Descemet's membrane was thickened. The endothelium was atrophied, and in places it could not be seen. There was a healed penetrating wound of the cornea at the limbus above. The posterior surface of this wound was occluded by dense connective tissue that blended with the iris stump above. This connective tissue extended along the posterior surface of the cornea for a distance of about 3 mm. Clinically it undoubtedly resembled an epithelial downgrowth. Its origin may have been from metaplastic endothelium, such as is seen as a response to the presence of free blood. The chamber angle was open below. Posteriorly, ganglion cells were present, although they were thought to be diminished. The optic nerve showed little atrophy. The nerve fiber layer was not thinned. It was thought that the thickening of Descemet's membrane and the changes in the endothelium, resulting

in bullous keratopathy, were aggravated by the anterior chamber hemorrhage.

CASE 8.—A 47-year-old white man developed glaucoma secondary to recurrent episodes of iridocyclitis. The intraocular inflammation subsided. His glaucoma resisted medical therapy, and its control required several surgical procedures. An intracapsular cataract extraction was performed in May, 1953. Postoperatively the vitreous face became condensed and secluded the pupil, causing the intraocular pressure to become elevated. This was reduced after a peripheral iridotomy and a subsequent needling of the vitreous face. His vision was corrected to 20/20. Although the tension has been intermittently controlled since June, 1954, the pressure at which the cornea becomes edematous has gradually decreased. Two years ago there was no evidence of corneal edema at tension levels of 40 to 50 (Schiøtz). Currently his cornea becomes edematous when the intraocular pressure is in excess of 25 (Schiøtz).

CASE 9.—A 53-year-old man had chronic glaucoma. His cornea was clear until the intraocular tension exceeded 60 units, (Schiøtz). He developed an occlusion of the central retinal vein, and the eye was enucleated. In flat preparation endothelial-cell concentration was 79 cells per high-power field.

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A New Magnetic Orbital Implant

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In this paper is presented a new magnetic orbital implant for use after enucleation which is expected to be a great improvement over all previous types. The implant contains a magnet, the active poles of which end directly under Tenon's capsule and conjunctiva. In this implant the magnet is placed so that it can exert considerable attractive force on the magnet in the prosthesis.

Since World War II many new implants have been developed, and the impetus for this must go to Cutler,* who designed the ingenious basket implant. In July, 1949,[3] was presented the first good orbital implant by one of us (O. H. E.) (Fig. 1). Allen published a report of a similar implant in May, 1950.[4]

Fig. 1.—Ellis orbital implant (1949).

The indications for enucleation and/or evisceration will not be discussed nor will the surgical anatomy, except as special technical procedures are involved.

Ophthalmologists have almost ceased using incompletely or partially buried implants. It has been proved conclusively over the years that unless an implant is entirely buried, with no portion protruding through the conjunctiva, sooner or later, even after a period of years, nearly all of the partially buried implants extrude. In fact, so great was the reaction of ophthalmologists to this unsuccessful procedure that many returned to the use of simple glass or plastic spheres in cases of enucleation.

To the best of our knowledge, with the use of buried plastic, either spheres or the earlier implant, no case of allergic reaction has developed. In a few patients allergy to the partially buried plastic apparently occurred and in some instances may have hastened the rapid extrusion. The methacrylate (Lucite) used in these new and the earlier types apparently rarely results in an allergic response.

A number of completely buried implants have been devised, but none has

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* References 1 and 2.

withstood the test of time so well as the one introduced by one of us (O. H. E.) in 1949. Comparatively very few of these have extruded either early or late. We have been informed unofficially that this was the type of enucleation implant used exclusively in one of our foreign "police actions," with excellent results.

Two modifications of the first implant have been in use for many years. Landegger made a slot posteriorly and tied in the oblique muscles. This had the effect of keeping the implant well forward in the orbit but apparently did not increase its motion. T. Moore used the implant with a threaded hole in the center, then, some weeks after healing had occurred, made an opening in the conjunctiva with cautery and threaded a tantalum screw into the hole. This gave excellent motion temporarily but later extruded. Recently Fine † has added a magnet in the body of the implant.

The incorporation of a magnet in the implant has been used in many types.[5] In our limited observation of a number of these others, the magnet has not increased the motion. One of the difficulties has been the weight of the metal in the prosthesis.

No implant can be adequately tested by one ophthalmologist or even by a group in such a large metropolitan area as Los Angeles. It is therefore our plan to present this as a preliminary report, since only after a number of years can any implant be adequately evaluated. Certainly many improvements in orbital implants are to come, and two of these forward steps along the road are now to be presented.

The first major change is in the back of the implant. The front ring has been kept the same, but the back is changed to a pyramid or cone shape (Fig. 2).

† Fine, M.: To be published.

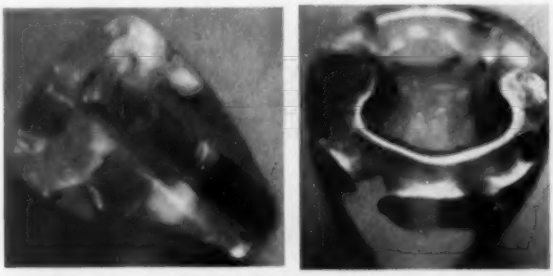

Fig. 2.—New magnetic orbital implant.

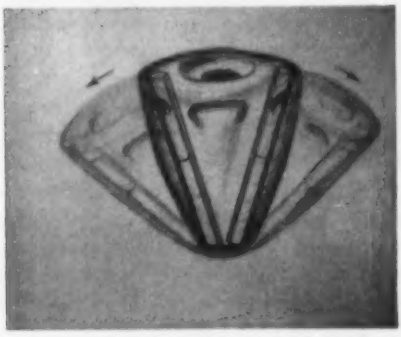

Fig. 3.—Fulcrum-type motion of implant.

The idea behind this is that the pyramid projects into the muscle cone and therefore has a more positive and definite action. This has proved to be true. The motion of the implant is due to the pull of the muscles moving the anterior portion of the implant, a fulcrum type of motion (Fig. 3). If you have observed the action of a partially buried or partly extruded implant, you will be convinced that this is so. The apex, or deepest part, of the implant remains fixed, and the top is moved from side to side or up and down by the action of the rectus muscles. Furthermore, the projecting posterior tip acts like a rudder, preventing the migration or tilting of the implant. An uneven front makes the fitting of the prosthesis more difficult and in some cases nearly impossible. A cone-shaped implant with the front covered with wire mesh has been devised by Berens.‡ This has not been previously used with the front ring or magnet.

The volume of the round-back implant was estimated, and this was found to compare exactly with the volume of the pyramidal-shaped implant. In my experience the 16.5 mm. implants are fully large enough for any orbit; however, some surgeons wish the larger sizes and so these also have been made. A few of the cones 25 mm. in length were inserted, but these were found to fill up the orbit so completely that only a small prosthesis could be worn. The motion, however, was excellent.

A number of the pyramidal-shaped implants have been in place for two years, and it is to be particularly noted that there is no tendency for the implant to tip or roll as in the case of the round-back implants. In one case done under less than optimum conditions one side became exposed. It was seen that the implant was not tipped, and so at operation Tenon's capsule and conjunctiva were dissected free and the implant successfully recovered. This implant has now been in place for many months, and there has been no further tendency for the implant to uncover or extrude. If this had been the former round-back type, this implant would have extruded rapidly; it would have twisted and one edge of the rim would have cut through immediately.

The second change is the insertion of the magnet.

With the help of Mr. Hubbard, of the Magnet Division of the General Electric Company, who had worked directly with us in every phase of the development, we have designed and produced a magnet which is light in weight but magnetically very strong, since it is essentially a long bar (Figs. 4 and 5). The old horseshoe and dumbbell shapes are much less efficient than a plain bar magnet. The metal is Alnico No. 5, and, since these are mass-produced for magnetic pick-ups, phonographs, recorders, etc., the cost is very small. These are permanent magnets, and the duration of action is apparently limitless. They have been in use for many years with no detectable decrease in power. Even should the magnetic force decrease they can easily be "recharged." After the implants are made up and the magnets are imbedded, the implant is placed in a magnetic field to bring the magnets to full capacity. The implant contains four of these small ($\frac{1}{8} \times \frac{3}{8}$ in.) bar magnets, end to end, bent in the middle to fit the implant, with a small bit of steel (a piece of old razor blade) as a "keeper" over the two ends at the back of the implant. One of the most important things we learned in the preliminary work is that the magnetic force increases inversely with the cube or more of the distance and correspondingly de-

‡ Berens, C.: To be published.

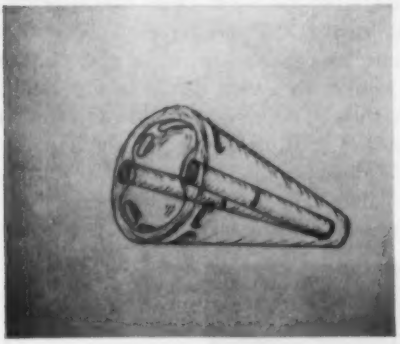

Fig. 4.—Diagramatic representation of new magnetic orbital implant.

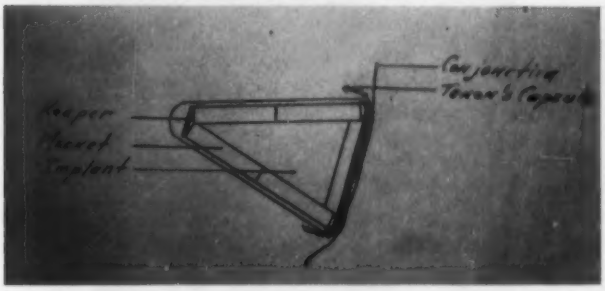

Fig 5.—Diagramatic representation oi new magnetic orbital implant.

creases with the same rapidity. It thus becomes obvious why the previous magnetic orbital implants failed to work. They were buried too deep to have any magnetic attraction. Also the other magnets were made from Alnico No. 2. The newer metal, Alnico No. 5, has a magnetic force three times greater than the No. 2 per unit of weight. In the front, the magnets end just barely under the surface, as shown in Figure 5. Since this is covered only by Tenon's capsule and conjunctiva, the ends of the magnet are only 2 to 3 mm. from the magnet in the prosthesis.

Upon examination of the implant it will be seen that there are six holes instead of the usual four. Also, the holes just above and below the ends of the magnets are slightly smaller than the superior and inferior ones. Since the magnets are brought to the top surface of the implant in the horizontal meridian, in the procedure the medial and lateral rectus muscle tendons are split, and separate sutures are placed in each.

In the manufacture of the ring-shaped implants, with either rounded or pyramidal posterior sections, the first product is a highly polished surface. It is felt that the rough or dull finish tends to be retained better and therefore it is recommended that they be used roughened, the polish removed. This is an extra step in the processing but is definitely worth while.

Procedure for Insertion of Implant

The enucleation is performed in the usual manner, with the following main points: The conjunctiva is incised at the limbus so as to preserve as much of it as possible. The conjunctiva and Tenon's capsule are then freed well back by blunt dissection. Each rectus tendon is isolated on a muscle hook and Tenon's

capsule is stripped off. This should be dissected far back from the insertion, as in doing a muscle recession, that is, at least 6 to 7 mm. from the insertion in the globe. A double-arm 0000 chromic absorbable surgical (gut) suture is placed in the tendon, with a catch or lock stitch added in the lateral bands. The tendon is then cut from the globe. A similar suture is placed in the tendon of the inferior rectus muscle. It is necessary to split the tendons of the horizontal muscles into two equal halves. This is done, and separate chromic sutures are put in each of the top and bottom halves before they are cut from the globe (Fig. 6). It is advisable to fasten each pair of sutures in turn to the

Fig. 6.—Muscle has been split; suture has been placed in lower half of lateral rectus tendon, already cut from globe. Suture is in top half of tendon, ready to be cut from globe.

drapes with a small hemostat after the suture is placed and the tendon has been cut from the eyeball. The enucleation is completed, and the hemorrhage is controlled with the Anthony orbital compressor. While the assistant holds the orbital compressor, the surgeon passes the sutures of the muscles into their corresponding holes, after first cutting off the needles. The orbital compressor is then removed, and the implant is put in the orbit apex down. It is then best to tie the suture from the top half of the medial rectus tendon to the bottom half of the lateral rectus suture (Fig. 7); then the bottom half of the medial rectus tendon suture is tied to the top suture of the lateral rectus. The sutures of the superior and the inferior recti are then tied over the previously tied tendons (Fig. 8). If possible, by gentle tugging and pulling, it is the best to have the muscle tendons themselves make the first loop around each other. Too strong a tug can easily pull the sutures out of the tendons, and so this should be avoided. After sutures are all tied, a few single stitches are put in the lateral bands or edges of the tendons. A purse-string suture of chromic gut is used to close Tenon's capsule, reinforced by single stitches

Fig. 7.—Top half of medial rectus tendon suture tied to suture from bottom half of lateral rectus.

Fig. 8.—Sutures of muscle tendons tied together.

where necessary. Interrupted black nonabsorbable surgical (silk) mattress sutures close the conjunctiva.

It has not been our practice to use a conjunctival stent immediately after surgery, and no reason can be seen for the use of one. It might help to create an opening in the conjunctiva, increasing the chance of extrusion of the implant. A mild antiseptic ointment is placed in the conjunctival sac and a firm head dressing is put in place as follows: An eye pad is placed over the lids; then a number of fluffed gauze squares are put on to form a mound about as big as a fist. Inch adhesive tape is applied as firmly as possible. Next a wide cotton gauze bandage is wound around the head; a gauze square is placed over the lower lobe of the ear and a mastoid type of dressing is put on, again wound very tight. This is further reinforced by additional adhesive over the front of the dressing and around the head. It is most important to have this pressure dressing stay in place for at least five days. If the patient complains, rather than loosen the bandage as much sedation and analgesia as necessary should be given the patient, thereby lessening the pain and complaints; however, too much pressure can cause edema of the scalp and constriction of the blood supply, and so this must be watched for. If the pressure dressing has remained in place from five to seven days, it will be gratifying to find that there is little or no edema of the lids or orbit when the first dressing is done. At this time a few gauze squares fluffed are placed over a new eye pad and additional pressure dressing, but with adhesive tape only, is applied. This dressing is in place for a second week with one or two changes. After a week or ten days the conjunctival sutures are removed, and in another few days, if there is little or no reaction, the initial fitting of the prosthesis can be started.

A method of fitting the prosthesis for this new magnetic implant has been developed which has proved to be successful in placing the magnet in the correct position, usually at the first attempt.

After healing is completed, the first step in the fitting of the prosthesis is to fit a prosthesis in the customary manner, insuring that it is properly centered and has the maximum motion in all directions. The prosthesis should be slightly smaller in the horizontal diameter and somewhat more curved. If the usual length of the prosthesis were used, much of the lateral motion would be stopped by rotation into the canthus.

The second step is removing as much of the plastic material as possible from the posterior surface of the prosthesis. The same type of small bar magnet, notched on one end, is placed in the orbit prior to taking the impression. The notch is only used to indicate the proper end corresponding with the

magnetic field of the implant. Any dental gelatin impression material which has high definition is satisfactory for this step (Jeltrate). This is prepared and poured into the orbit with the magnet in place. The patient looks straight ahead. The lids are held back out of the way, and the prosthesis is used as the shell to hold the impression material. After the material has hardened, which is usually within two minutes, the prosthesis is removed from the socket and, as a general rule, the magnet will come out with the impression. However, it is of no importance if it does not, as the notch will be clearly defined in the impression material. In one of our early cases, the pole of the magnet in the prosthesis was accidentally reversed. After the prosthesis had been in place for a few minutes the magnetic force was strong enough to turn the prosthesis completely around (rotated 180 degrees).

A negative plaster mold is then made of the prosthesis and the gelatin impression material. The prosthesis is then finished with an opaque or clear plastic to take the place of the impression material, with the magnet imbedded in the plastic (Fig. 9).

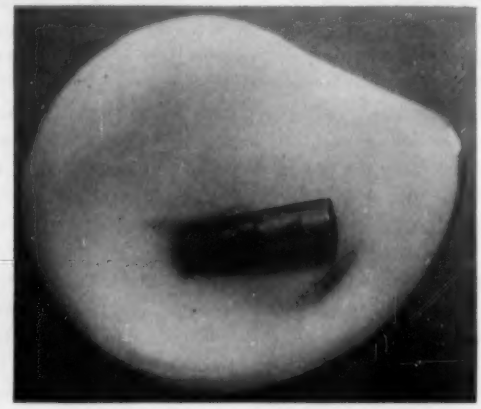

Fig. 9.—Magnet imbedded in posterior surface of prosthesis.

It has been found that in order to secure maximum motion it is necessary to remove the major portion of the plastic added in place of the impression material. Apparently the reason for this is that when the socket in the primary position is filled with the impression material no room is left for the prosthesis to move when the socket changes shape, as it does in movement from side to side. This flat projection, which contains the magnet, seems to form an indentation in the conjunctiva, which actually places the magnet of the prosthesis closer to the magnet in the implant. So far, in the cases we have seen, this protrusion does not increase socket secretions, as would normally be expected. The possible explanation of this may be the lack of friction by the knob, because it is held rigidly in place by the strong magnetic force.

These implant magnets are so strong that a magnet in the prosthesis may not be necessary. As far as is known at this early date, steel or metals of similar physical properties may be used in the prosthesis instead of a magnet, without lessening the efficiency of the prosthesis-implant relationship. This results in decreasing the weight and bulk of the prosthesis, eliminating the sagging of the lower lid, which had to bear the weight and bulk of the magnets of previous

types. The use of other magnets and metals in the prosthesis is still under investigation. In these first cases it has been found that it takes 20 to 30 minutes after insertion for the prosthesis to "settle" before maximum good movement is obtained. This latent period would be expected to decrease or disappear after the prosthesis has been worn for many months.

In considering the problem of extrusions, these should be divided into early, or immediate, and late. In the first category must be included faulty suturing of the muscle tendons. Also, it must be noted that the implants come out through the suture lines in Tenon's capsule and conjunctiva. This point, the elimination of extrusion, is one of the most important of this presentation, because no secondary implant is ever as successful as the primary (immediately following enucleation). The motion of the implant placed secondarily is always less, probably owing to increased scar tissue and/or shortening of the muscle tendons. This, plus the decrease in the amount of conjunctiva, greatly diminishes the movement of the prosthesis. Also, probably owing to the loss of conjunctiva, the lid conformation in the secondary implant is frequently poor. Thus, since many secondary implants also extrude, it behooves us to take particular pains to prevent extrusion by all possible means.

In operating on late extrusion of orbital implants of our own and others, it has been noted that the muscle tendons that have been tied over the front of the implant have become part of the scar tissue and are not discernible as separate structures. The muscles have been identifiable only considerably below the top of the implant. Thus, the tendons have apparently joined with Tenon's capsule to form a scar tissue mass covering both the body and the ring of the implant. It is our feeling that extrusions have come about by slipping or twisting of the implant, and the comparatively sharp side then cuts its way through this scar tissue. In the last extrusion operated upon, there was definitely no difference in the forward position of the lateral and medial recti, although the implant had twisted and presented nasally. In placing secondary implants after extrusions, replacements of round glass or plastic implants, this fact must be kept in mind, that the muscle tendons anteriorly are not discernible, and one must go well back to find them. This is probably the most important reason why many secondary implants fail, that tissue anteriorly is mistaken for muscle tendons; a suture is put in this and tied. This tissue, of course, will promptly slip, allowing the implant to twist and extrude. This idea of the scar tissue anteriorly covering the implants, to our knowledge, has not been described elsewhere. It certainly must be true, as confirmed by the use of the round glass or plastic spheres. When these were used, all the operafor did was to cut the muscles from the globe and put a purse-string suture into Tenon's capsule. These spheres had excellent motion, but unfortunately there was nothing to transfer the motion to the prosthesis. Certainly the anterior one-third or half was Tenon's capsule and scar tissue, and well back along the side was the position of the rectus muscle attachment. Bringing the tendons over the front of the sphere did not help the situation in any way. There was still excellent motion of the ball but little or none of the prosthesis. And again then, as now, in our more recent surgery with the front ring implants, scar tissue occurred, incorporating Tenon's and the rectus tendons, and the active part of the muscle was effective well down on the side of the implant. Many contend that a muscle tendon slipping is the reason for the twisting and extrusion. In our opinion, this rarely happens. Possibly it is the pressure of the prosthesis on the

implant that causes it to twist. Then, when it does, it rapidly cuts its way through this scar tissue and extrusion occurs. This is avoided with the cone-shaped implant. In our experience, if the implant stays straight without twisting in the orbit it does not extrude.

At this early stage it is premature to come to any conclusions regarding this very strong magnet that has been added to the implant. If it is found to be too strong, its strength can be diminished in many simple ways. The only complication that can be foreseen is the possibility that erosion of the conjunctiva might occur.

Improvements in surgical technique, antibiotics, and cortisone have decreased the number of enucleations performed, but there are still the occasional surgical failures, the untreated or unsuccessfully treated glaucomas, malignant melanomas, and many other conditions in which enucleation is indicated. The two important steps in the advancement of our knowledge of the orbital implants are (1) the combination of the ring anteriorly with the cone posteriorly, which should greatly decrease extrusion, and (2) the development of a strong magnet in the implant placed so that the active ends produce an effective magnetic force for moving the prosthesis with an embedded magnet.

These implants have been in place 12 months to date. The motion is considerably better than that of any other buried implant and is as good as was obtained by using the integrated or partly buried implants before they extruded. The motion is better than implants in evisceration. It is to be emphasized that this is a preliminary presentation, since only after a number of years can any implant be fully evaluated. Should this implant continue to give such excellent motion—and we can see no reason for complications—we may be near our goal of having a simple buried implant for use after enucleation which will produce excellent motion in the prosthesis.

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Retinal Vasculitis with Intraocular Hemorrhage

Classification and Results of Special Studies

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Retinal vasculitis with intraocular hemorrhage may be defined as a series of related entities which affect the eyes of young persons, principally males. The principal form of this disease was first discussed adequately by Eales [1] and is characterized by spontaneous hemorrhages into the retina and vitreous which vary in severity. Roughly one-half of the cases of this type are thought to be bilateral. Gradual clearing of the hemorrhages may be followed by repeated relapses with subsequent retinitis proliferans, retinal detachment, cataract, and absolute glaucoma. Spontaneous subsidence of the disease after two to four years with varying modifications of vision may occur. Some association of the ocular disease with pulmonary or extrapulmonary tuberculosis has been observed in many of the cases reported in the older literature.

Examination of patients having the primary type of this disease usually shows disease of the peripheral retinal veins. There is sheathing of the vessels and variation in caliber of the smaller veins, with a tendency to form new vessels and saccular aneurysms. Peripheral retinal, preretinal, or vitreous hemorrhages may be present, and in many cases they are recurrent. In a number of instances the patient may be completely unaware of disease in the second eye, and examination shows involvement of the peripheral vessels; frequently the veins are engorged, and at times there is obvious beading at the site of a low-grade inflammatory process.

Healing is accompanied by absorption of the exudates and the intraretinal and vitreous hemorrhages. Recurrence of such bleeding is accompanied by new-vessel formation with secondary connective tissue proliferation in the retina and adjacent vitreous. Contraction of this tissue may lead to detachment of the retina.

Etiology

Early opinions as to the etiology were speculative. Of the conditions considered most likely during recent years, only tuberculosis has maintained its position. Many patients have been reported, however, in whom the diagnosis of tuberculosis could not be established and the etiology was in doubt.

The following are considered as possible etiologic factors:

Tuberculosis.—Tuberculosis has been considered as the prime cause of the disease for many years, and reports are available presenting the simultaneous

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existence of possible tuberculous lesions elsewhere in the eye or the actual existence of tuberculous lesions elsewhere in the body. A number of other reports have described the subsequent development of active pulmonary tuberculosis one to three years after onset of the ocular lesions. The older reports dealing with coexistent ocular disease and pulmonary tuberculosis impress one with the possible relationship between the two conditions. Most pathologic examinations of eyes have been made in advanced cases; therefore one might expect all trace of any specific etiologic agent to have disappeared. A number of eyes examined in the earlier stages have not demonstrated lesions which would suggest tuberculosis. Only two eyes have been reported which showed acid-fast bacilli (see below).

In many reported cases the diagnosis of tuberculosis has been made by exclusion, the evidence afforded by a positive tuberculin reaction, improvement on therapy with tuberculin, or a focal reaction to tuberculin.[2] Most of these observations are found in the older literature, and it is not certain how significant such findings would be at the present time.

The failure of a number of cases to respond to specific antituberculous therapy suggests either that the disease is not always due to an active tuberculous infection or that the agents are not able to reach and eradicate the infection.

It has been suggested that the retina or its vessels somehow become sensitized to tuberculoprotein and that the disease results from a hypersensitivity reaction. As an example of this, the case of Muncaster and Allen,[3] in which a previously healthy young woman developed a bilateral iritis following a tuberculin test of 0.005 mg. of purified protein derivative is of interest. Other similar cases have been reported, and we believe that the uveal tract or retina somehow becomes sensitized to tuberculoprotein; later ingestion or administration of a similar protein, regardless of its source, may lead to an inflammatory reaction. Intradermally administered tuberculin given during the course of the retinal disease frequently has resulted in exacerbation of the inflammation. Such reactions have been interpreted as indicating the specific etiology of the ocular disease, but in view of the ocular inflammation incited by tuberculin in healthy persons it is difficult to determine the significance of such reactions.

In spite of these arguments there is, however, reasonable proof that tuberculous infections play some part in the causation of retinal vasculitis with vitreous hemorrhages. Ample evidence is also at hand that other etiologies are important. To quote Duke-Elder, "It is not a disease entity but a clinical manifestation of many diseased conditions."

Thromboangiitis Obliterans (Buerger's Disease).—Marchesani[4] first suggested a relationship to this condition. His observations were based on the associated subjective changes in temperature and numbness of the extremities, absence of pulsation in the dorsalis pedis arteries, and trophic disturbances or gangrene of the lower extremities. It has been pointed out (Schmid[5]), however, that many people have subjective skin temperature and sensation changes in the extremities and that frequently peripheral pulsations in the dorsalis pedis arteries cannot be detected. The only finding of value in this group of cases would be trophic disturbances in the extremities or gangrene—and this has been encountered with great rarity in this disease. Schmid was unable to find any relationship in his 25 cases to thromboangiitis obliterans. Most observations on the peripheral circulation in this disease have been negative.

Focal Infection.—Rare cases have been reported in which there was a more

than a seeming relationship between a focus of infection in one portion of the body and the ocular disease and in which eradication of the focus seemed to eliminate recurrences of the ocular disease. Those favoring focal infection as a cause of this condition have gradually decreased in number over the years, as judged by the paucity of such reports in the past 10 years.

Congenital Abnormality of Venules of Retina.—A congenital abnormality or weakness of the retinal venules might predispose to development of this disease in some persons. Against such a possibility is the rarity with which abnormalities of this exact type are seen in routine examinations, although they may have been overlooked. One of our cases (Case 18), which is discussed later in this paper, showed abnormality of the venules in the uninvolved eye, which could be interpreted as a congenital lesion.

Other Etiologies.—Many other etiologies have been discussed in the literature, and therapy has been designed to eradicate the supposed causative agents, but they have not withstood the test of time.

Clinical Manifestations and Pathogenesis

For many years it was considered that the hemorrhages which occurred into the vitreous came from lesions in the ciliary body. Later, as observers became more skillful, it was accepted that localized retinal vascular lesions accounted for the entire picture.

As the result of our studies an impression is obtained that confusion has arisen from lack of a satisfactory classification of the entities comprising Eales' disease, retinal periphlebitis, recurrent vitreous hemorrhages, and retinal vasculitis. We prefer the term "retinal vasculitis," because the changes are not always limited strictly to veins and exact proof that the disease always affects the perivascular spaces of the veins is lacking. We would add to this title the clause "with intraocular hemorrhages" for those cases occurring in younger persons in which spontaneous vitreous hemorrhages constitute the dramatic onset of the disease.

Classification

A. Primary Retinal Vasculitis.—The initial lesions involve the peripheral retinal veins in a large percentage of cases. At the onset there is blurring, followed by spontaneous recurrent vitreous hemorrhages in one or both eyes during a period of time which may last from 1 to 10 years. Spontaneous remission may occur, with moderate visual damage; in other cases relentless recurrences may lead to organization of the vitreous by fibrovascular membranes, retinal detachment, and severe glaucoma. Occasionally the initial lesions commence in the larger veins, in which case the course is apt to be more disastrous because of concomitant involvement of the optic disc and macula.

Ophthalmoscopic examination in the earliest stages rarely has been recorded, but there seems to be general agreement that in most cases the peripheral veins in one or more quadrants of the retina are affected. The initial manifestation is an apparent vasculitis, with accumulation of exudate in and around the vein. Initially the lesion is soft, diffuse, and slightly elevated. The focus later becomes organized by scar tissue and develops a whitish appearance. Intraretinal and preretinal hemorrhages are frequently associated with this inflammation, and intraretinal edema is present. Occlusion of a larger vein leads to stasis with secondary telangiectasis. As a result, attempts to form shunts may occur.

This form is commonly described under the category of spontaneous hemorrhages into the vitreous in young adults. From a pathogenetic standpoint it is curious that the causative agent should pass through the arterioles and capillaries in order to affect the small peripheral veins. Another idea, with great merit, was first proposed by Fleischer [6] and has been supported subsequently by experimental observations. According to this method of involvement, the agent is liberated from the ciliary body and transferred via the intraocular fluids to the peripheral retina. In this manner the possible initial lesions in the perivenous spaces could be explained. At any rate, it is logical to assume that the agent affects the wall of the vein, producing a diffuse inflammation, resulting in more or less destruction and necrosis and at times in rupture and extensive bleeding. If the inflammation is such that it interferes with the function of the vein only, intraretinal hemorrhage and exudation may occur.

B. Secondary Retinal Vasculitis.— In this type the primary focus of the disease is in the ciliary body. The patient first complains of symptoms of anterior uveitis, and on examination the usual signs of iridocyclitis are present. Many such examples have been reported in the European literature, and occasional ones have been recorded in North American publications.

Within a short period after the onset of the cyclitis, a more or less localized retrograde extension occurs into the peripheral retina, involving the venous system, in many cases as far back as the equator. After subsidence of the disease, perivascular venous sheathing and retinal atrophy are observed. Saccular swellings and neovascularization are common. If the inflammation spreads, the smaller arterioles become secondarily affected and show sheathing and tortuosity.

C. Postchoroiditic Retinal Vasculitis.—This form requires only a brief description. It not uncommonly follows choroiditis in which there is secondary retinal edema and inflammation. In such an event the retinal veins and arteries become somewhat tortuous, vary in caliber, and develop perivascular sheathing. Such an occurrence is not uncommon in retinopathies as Coats' disease. Rarely, erosion of the retinal vessels by a focus of chorioretinitis results in hemorrhage.

Differential Diagnosis

Very few vascular diseases produce exactly the same manifestations as the primary and secondary forms of retinal vasculitis. A few entities resemble each form:

Primary Retinal Vasculitis.—The following clinical entities must be differentiated from primary retinal vasculitis:

Peripheral Chorioretinitis: The circumscribed irregular distribution of the lesions, the absence of specific involvement of vessels, and the lack of hemorrhages serve to distinguish the two. Frequently the patient is older, and oftenest only one eye is involved.

Coats' Disease: The primary involvement of the outer retina in a hemorrhagic or exudative process and the absence of vitreous hemorrhages assist in the diagnosis. The patients are usually much younger, and the disease is characteristically unilateral.

Von Hippel's Disease: The enlargement of a principal artery and vein leading to a sector of the fundus and the observation of a localized tumor serve to differentiate the two conditions. At times, however, secondary changes in the tumor and retina produce edema, hemorrhages, and retinal elevation, which

suggest a vascular inflammation. Oftenest one can detect the enlarged vessels or tumor, which suggests the proper diagnosis.

Diabetic Retinopathy: The history, clinical studies, bilaterality, and diffuse vascular involvement serve to differentiate the two conditions.

Central Retinal Vein Thrombosis: The vasculitis in this condition may affect the central retinal vein and cause the manifestations of central retinal vein thrombosis (Verhoeff and Simpson[7]). The extensive preretinal and vitreous hemorrhages of retinal vasculitis are lacking, however, probably because the larger vessels are more resistant to necrosis or because the inflammation affects the vein within the substance of the optic nerve. A number of cases have been reported in which the involvement has occurred in the larger veins near the disc, resulting in a picture resembling tributary thrombosis; the same eye often shows the typical peripheral vasculitis.

Secondary Retinal Vasculitis.—The following clinical entities must be differentiated from the secondary type of retinal vasculitis:

Choroiditis: A number of reports discuss the secondary retinal involvement which occurs in Jensen's choroiditis juxtapapillaris and other forms of choroiditis. It is not unusual to see secondary perivascular sheathing, variation in caliber, tortuosity, and edema in association with such lesions. At times the evidence as to the existence of a focus of choroiditis is scanty, and one may have difficulty determining the actual nature of the retinal vascular disease until there is complete healing.

Pulseless Disease: This condition may result in extensive vascular changes in the region of the disc and remaining fundus. The associated systemic findings exclude it from consideration.

Pathology of Eales' Disease

A review of the literature * shows 18 pathologic reports of retinal vasculitis. A summary of these pathologic reports shows that seven cases † had an associated granulomatous iridocyclitis or choroiditis (secondary vasculitis), and the tissue in these cases showed the inflammation in the perivascular space to be granulomatous in nature.

In all the other reported cases the vasculitis of the retina was not associated with any other ocular inflammation. The pathologic picture, however, varied. Elliot[24] found cuffing of the retinal venules in an eye removed six months after onset of the disease, but he did not believe that it was a true inflammatory periphlebitis. Ballantyne[20] described the cellular exudate within the vessel wall and thought that the change was consistent with a phlebitis; in the remainder, the inflammation was composed solidly of chronic inflammatory cells. In all the cases except that of Elliot the disease process was of long duration and the eyes were removed because of the secondary glaucoma.

Acid-fast organisms were found by two authors. Stock[9] demonstrated acid-fast bacilli in the peripheral retinal lesions, and Gilbert[10] found the similar organisms in the perivascular sheath of an affected retinal vein.

Various attempts to reproduce periphlebitis in experimental animals have failed. However, this condition did occur in 1 of 46 animals in which tubercle bacilli were injected into the homolateral carotid artery by Finnoff.[25] This same rabbit also developed iridocyclitis.

* References 6 and 8-24.

† References 6, 8, 11, 14, 16, 21, and 22.

Pathologic Studies.—During the past year 19 eye specimens with the clinical and pathologic diagnosis of Eales' disease or periphlebitis of the retina were collected from various institutions.‡ The pathologic lesions which were observed in the retina could be divided into two groups: (1) primary vasculitis and (2) secondary vasculitis. The eyes exhibiting primary vasculitis seemed to show the initial changes in the retinal venules and to be without other evidence of ocular disease. The eyes showing secondary vasculitis of the retina had an associated uveitis, and the inflammatory changes in the retinal venules appeared to be secondary to the initial infection.

Of the 12 eyes with probable primary vasculitis of the retina, only 4 demonstrated a granulomatous inflammation around the retinal venules. In all the other eyes the inflammation was of a nonspecific type.

The clinical histories of the patients with eyes having primary vasculitis were similar. The ages varied between 26 and 40, and three-fourths were men. There was usually a history of a spontaneous vitreous hemorrhage which gradually cleared, only to be followed by subsequent hemorrhages. Over a period of years an initial peripheral periphlebitis was followed by recurrent intraretinal and vitreous hemorrhages, extensive retinitis proliferans, retinal detachment, and, as a terminal event, the development of intractable glaucoma.

Several of the cases here developed a secondary cataract. Removal of the cataract in two cases resulted in recurrence of the vitreous hemorrhages. The glaucoma which occurred did not respond to x-ray therapy, diathermy, cyclodialysis, trephining, or iridencleisis operations.

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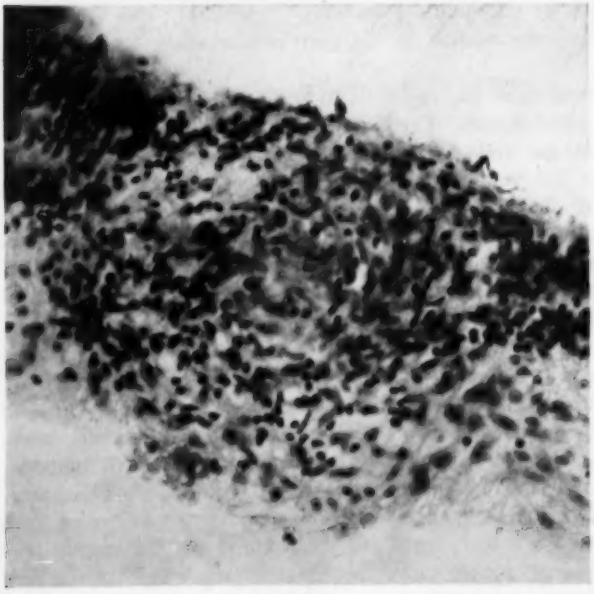

Fig. 1.—Granulomatous vasculitis of the retina (primary type).

The pathologic changes in the group of eyes enucleated for primary periphlebitis were similar. There was usually a complete funnel-shaped detachment of the retina (Fig. 1). In four of the cases there was a granulomatous inflammation of the peripheral retinal veins and rather marked disruption of the normal architecture of these vessels. The surrounding perivascular tissue was infiltrated with epithelioid cells and lymphocytes. There were, however, no evident giant cells. Proliferation of the endothelial cells of the venules was also seen (Fig. 2). Special stains failed to reveal an etiologic agent.

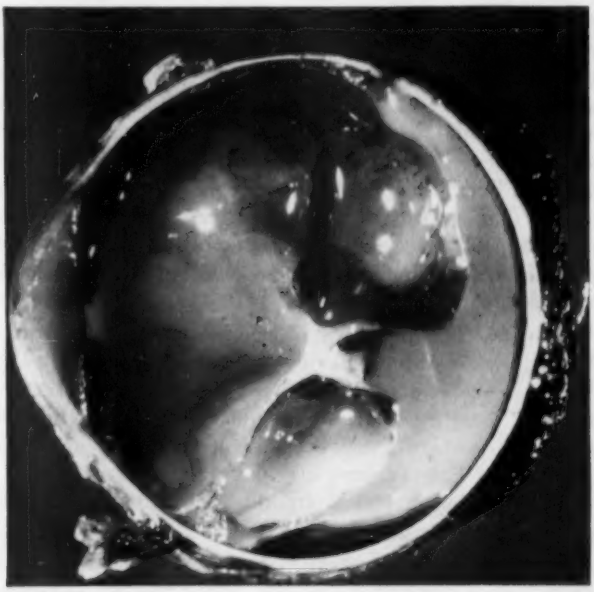

Fig. 2.—Photograph of gross specimen. Late stage of primary retinal vasculitis with vitreous hemorrhage, retinitis proliferans, retinal detachment, and glaucoma.

In eight of the primary periphlebitis cases there was no evidence of a granulomatous inflammation, the principal change consisting in a perivascular infiltration with lymphocytes. There was slight proliferation of the endothelial cells and also thickening and hyalinization of the vessel wall. In all the cases the retina was detached as the result of contracting bands of connective tissue extending into the vitreous from the retina. There usually was marked degeneration of the retinal stroma with secondary gliosis and hyalinization of the tissues. The retinal arterioles were sclerotic. This finding is not considered as specific for retinal vasculitis, because degenerative arteriolosclerosis is commonly found in retinal detachments of long standing. In several cases there was degeneration of the lens cortex. In all the cases anterior peripheral synechiae obstructed the angle. The majority demonstrated a fibrovascular membrane extending over the anterior surface of the iris which resulted in various grades of ectropion uveae.

In six of the eyes the vasculitis of the retinal venules was secondary to uveitis. Four of the six specimens showed a periphlebitis of the retinal venules, secondary to a chronic granulomatous chorioretinitis. An etiologic agent was not demonstrated, but the pathologic changes in one case were suggestive of toxoplasmosis. In one case of keratitis and iridocyclitis, the periphlebitis of the retina was due to the extension of the inflammation posteriorly. In another speci-

men the retinal changes and vitreous hemorrhages were attributed to occlusion of the central retinal vein and did not represent a primary or a secondary vasculitis. In still another specimen there was an ectopic lens and the patient demonstrated the usual clinical features of the Marfan syndrome. It was felt that the vitreous hemorrhages were secondary to the degeneration of the retina. The inflammation surrounding the retinal venules in this secondary type of periphlebitis was nonspecific.

A conclusion which may be drawn from these pathologic studies is that a primary vasculitis of the retinal venules does not present a characteristic pathologic picture. However, the pathologic changes may be considered in three stages: (1) the retinal vasculitis stage; (2) the retinal detachment stage; (3) the glaucoma stage. The pathologic changes in the retinal vasculitis stage are not always similar. The late stages of the disease are grossly identical. The retinal detachment and the glaucoma stage are purely secondary to the organization of the vitreous hemorrhage with subsequent retinal detachment. Pathologically this is also seen in diabetes, retrolental fibroplasia, and vitreous hemorrhages of traumatic origin. The secondary glaucoma is the result of an angle block. Anterior peripheral synechiae secondary to a retinal detachment are probably the result of two factors: the anterior displacement of the iris by the blood-filled vitreous and the secondary chronic iridocyclitis.

A number of the eye specimens examined demonstrated a late stage of the disease process with such extensive scarring of the retina that the initial pathologic change in the retinal venules could not be determined. It is conceivable that in some of these cases the initial inflammation may have been granulomatous in nature. It is also felt that the presence of recurrent vitreous hemorrhages in the late stage of Eales' disease may not signify persistence of an active inflammation in the retina but may arise from the breakdown of the fragile neovascular tissue extending into the vitreous.

A specific etiologic agent in primary vasculitis of the retina was not demonstrated. It is conceivable, in view of the variable pathologic picture of vasculitis of the retina, that the etiology may be variable.

Treatment

A satisfactory regimen for control of retinal vasculitis has not been evolved. Certain types of therapy are indicated, however, for possible causative agents.

1. Primary Retinal Vasculitis.—Antituberculous Therapy: Inasmuch as many cases have had associated ocular or systemic infections or have developed tuberculosis within a period after onset of the ocular disease, one should always be aware of the necessity of treating such cases as forms of ocular tuberculosis, in spite of negative clinical findings. In our series, antituberculous therapy did not alter the course of the disease. The indiscriminate use of the antituberculous drugs is not only unnecessary but wrong. If therapy is indicated, we generally commence with streptomycin 1 gm. intramuscularly three times a week, isoniazid isonicotinic acid hydrazide, 100 mg. three times daily (or aminosalicyclic acid 10-12 gm. daily) by mouth for a four- to six-month period. Doubtful and suspicious pulmonary or extrapulmonary infections should be treated accordingly by a physician who specializes in pulmonary tuberculosis. The cooperation of a person experienced in the management of such tuberculous cases is invaluable.

General Management: A good internist or general practitioner should regulate

the habits, diet, rest, and general condition of the patient. Any foci of infection or circulatory disturbances should be corrected.

Treatment of the Ocular Lesions: (*a*) Radiation therapy: This form of therapy was advocated by Guyton and Reese [23] for recalcitrant cases with recurrent hemorrhages. Our experiences with such cases, and that expressed to us by others, has been disappointing.

(*b*) Diathermy: Franceschetti and Forni [26] and Franceschetti [27] have advocated diathermy coagulation of the affected peripheral inflammatory foci in an effort to cause scarring and shrinkage of the neovascularized areas. The surgical intervention in these cases was performed on cases which had not yet developed vitreous hemorrhages (prophylactic) and on those with many vitreous hemorrhages (therapeutic). These authors operated on the second eye in five cases after loss of the first eye through previous hemorrhages, with apparent good success. Such surgery depends upon the ability to locate the affected vessels and to direct the diathermy accordingly.

II. Secondary Retinal Vasculitis.—Those cases with cyclitis and secondary retinal involvement are the most important to consider therapeutically. The usual treatment for cyclitis should be instituted, such as cycloplegics and steroid therapy. In the event of failure after the usual measures, one should institute antituberculous therapy, as previously described. This should be combined with corticosteroid therapy. We ordinarily administer cortisone, hydrocortisone, or prednisone (Meticorten) in the proper dosage, and in the event of failure in immediate response we increase the dosage. Subconjunctival injections of these steroids may also be given in an effort to control the inflammation, usually in a dose of 0.5 cc. of the suspension high up under the upper lid.

Analysis of Cases

A total of 21 cases of retinal vasculitis with intraocular hemorrhage were studied. A great majority of these cases were referred to our Uveitis Survey Clinic for study. Four were hospitalized, and special blood examinations,§ which will be enumerated, were done to determine if any abnormality of the hemostatic mechanism of the blood could be found. The various factors which cause hemorrhage were reviewed, and special determinations were done as a preliminary study. The accompanying Table summarizes the findings.

The median of the earliest age at onset of the disease in either eye was 33 years. The earliest age of onset of the hemorrhage was 19 years, and the latest was 57 years. At the time of the initial visit the disease had existed anywhere from a few weeks to 15 years.

Females were affected in only 4 of the 21 cases. The preponderance of males in this series agrees with that recorded by other authors.

Follow-up examinations were not possible on many of our cases, because they were referred from distant areas. Of those we were able to follow, recurrent hemorrhages had occurred in most cases. The visual acuity varied according to how recently the vitreous hemorrhage had taken place.

The records of the patients that were referred to our uveitis clinic (19 cases) contained the following data: (1) detailed medical and ophthalmic history; (2) complete physical examination; (3) detailed examination of the eyes, including

§ Dr. Jonah Li, of the Department of Medicine, assisted us in conducting this phase of the study.

Summary of Cases of Retinal Vasculitis with Intraocular Hemorrhage

Case	Age	Sex	Age of Onset		Visual Acuity		Hemorrhage	Type of Vasculitis
			R.E.	L.E.	R.E.	L.E.		
1	20	M	19	20	20/70	20/40	Once	Primary
2	34	M	32	22	20/70	20/70	Two recurrences	Primary
3	39	M	38	38	20/40	HM	Multiple recurrences	Primary
4	32	M	30	29	20/70	LP	Multiple recurrences	Primary
5	57	F	48	57	No LP	20/20	Once	Primary
6	38	M	..	38	10/200	20/20	Once	Secondary
7	41	M	..	40	20/15	20/30	Once	Primary
8	50	M	50	42	20/50	HM	Multiple recurrences	Primary
9	36	M	33	33	20/100	20/200	Once	Secondary
10	43	M	36	36	HM	20/20	Multiple recurrences	Primary
11	47	M	38	38	20/30	20/30	Multiple recurrences	Primary
12	32	M	31	31	20/200	20/20	Multiple recurrences	Primary
13	27	F	..	27	20/20	20/30	Multiple recurrences	Primary
14	24	M	20	24	20/20	20/50	One recurrence	Primary
15	35	M	32	..	20/30	20/20	One recurrence	Secondary
16	30	M	29	..	20/100	20/20	Once	Choroiditic
17	59	F	..	57	20/20	HM	Two severe recurrences	Choroiditic
18	44	M	44	..	CF	20/30	Multiple recurrences	Primary
19	30	M	30	24	LP	20/20	Multiple recurrences	Primary
20	35	F	34	..	10/200	20/15	Once	Primary
21	35	M	..	29	20/20	20/20	One recurrence	Choroiditic

slit-lamp biomicroscopy and ophthalmoscopy with pupils dilated; (4) skin tests, including the tuberculin, Frei, toxoplasmin, coccidioidin, histoplasmin, and brucellergin tests; (5) serologic tests, including the Toxoplasma dye test, the Toxoplasma complement-fixation test, Brucella agglutination and complement-fixation tests, Q-fever complement-fixation test, and Kline and Kahn tests for syphilis; (6) white blood cell count and differential count; (7) sedimentation rate, and (8) roentgen chest examination and special films when indicated.

Special attention was paid to tuberculosis because of the strong evidence in the literature that retinal vasculitis may be due to tuberculosis. None of the 21 cases had any evidence of active tuberculosis on physical examinations or by chest x-ray. Only 3 of the 21 patients gave a positive history of contact with tuberculosis. The results of the tuberculin tests showed that 16 patients had positive reactions to first-strength PPD; three patients had positive reactions to second-strength PPD; two patients who had negative tests with first-strength PPD, but second-strength PPD was not given to them.

Investigations

Special studies were performed to determine if any of the following known causes of spontaneous bleeding were present in this group of patients (Wintrobe).

1. Trauma to the blood vessels by direct injury or by erosion from a pathologic process. This is probably the commonest cause of hemorrhage. There were several examples of this type of intraocular hemorrhage in our series. One case

was originally seen with a vitreous hemorrhage which appeared to be due to a periphlebitis. Follow-up studies now show that there are healed chorioretinal lesions along the inferior temporal retinal vein, which were probably the cause of the vitreous hemorrhage due to erosion of the retinal vessels.

2. Vascular dysfunctions due to ascorbic acid (vitamin C) deficiency. Ascorbic acid level in the blood was studied in four of our cases. All determinations were normal except that of one patient, who had an ascorbic acid level of 0.37 mg. per 100 cc. The normal value, as determined by Dr. McIvor, of the Department of Pathology, ranges from 0.5 to 1 mg. per 100 cc.

3. Tests to determine altered coagulability of the blood: (*a*) Electrophoretic analysis of blood plasma was performed in five cases. Fibrinogen deficiency is a rare cause of bleeding, and it was unlikely that the cases in this group were due to this deficiency. We were perhaps concerned more with abnormal fibrinogen than with deficiency. The five cases studied did not reveal any consistant abnormal protein pattern in the plasma.

(*b*) Hypoprothrombinemia (prothrombin time). Bleeding tendencies are seen when the prothrombin level in the blood is depressed, such as with vitamin K deficiency and liver damage. Prothrombin time determinations were made in four of these cases, and all were within normal limits.

(*c*) Platelet count: Platelet counts were made in 5 of the 17 cases, and all were within normal limits. The normal count ranges from 350,000 to 550,000 per cubic millimeter.

(*d*) Bone marrow biopsy: Bone marrow studies were performed on four cases to see if there was any evidence of depression of the megakaryocytes, which are precursors of the blood platelets. The decrease or depression of the megakaryocytes ordinarily should be followed by a corresponding change in the number of circulating platelets. Since the platelet count was normal in every instance, it was unlikely that we would find pathology of the bone marrow. These biopsies showed a nonspecific hyperplasia of all the elements, with no evidence of depression or decrease of the megakaryocytes.

Comment

The special blood studies were done on selected patients with primary retinal vasculitis having vitreous hemorrhage. The purpose was to determine if there was any consistent abnormality in the hemostatic mechanism of the blood. The determinations were primarily designed to see if there was any defect in the blood coagulation mechanism. The ascorbic acid level determinations would be most indicative of one form of vascular dysfunction. We are aware of the fact that bleeding cannot take place unless there is a vascular dysfunction, regardless of the status of the blood coagulation mechanisms or of the platelets. However, some hematologists feel that there are types of bleeding that are due purely to thrombocytopenia, or purely to altered coagulability of the blood. It must be assumed in these cases that there is a concomitant increase in capillary fragility. The blood pressure cuff test (the Rumpel-Leede test) was performed in four of our cases, but, since it was uniformly negative, it was discontinued.

After reviewing the literature and completing a careful ophthalmic examination and laboratory studies, we seemed to be able to classify the cases into definite groups. This helped us to understand the disease and assisted us in determining the prognosis. This classification has been presented in the first part of this paper.

Primary Retinal Vasculitis.—Fifteen of the twenty-one cases were examples of primary vasculitis. All except three of these cases showed bilateral involvement. Ten of the fifteen patients had follow-up studies ranging from less than one year to four years, and all showed progression of their disease. Most of the patients had recurrent hemorrhages, and ophthalmoscopic examination invariably showed more extensive vasculitis when the fundus could be visualized. In one patient (Case 4) ophthalmoscopic examination revealed that the vasculitis involved mainly the arterioles. In two other patients (Cases 2 and 12) ophthalmoscopic examination revealed that the arterioles and venules were involved equally.

In one of our cases (Case 18) with vitreous hemorrhage in one eye, the patient thought that the opposite eye was normal. Detailed ophthalmoscopic examination revealed marked dilatation ("beading") of the superior and inferior temporal veins in the midperiphery of the fundus. There was no sheathing, and hemorrhages were absent.

Although hemorrhage is an inevitable part of retinal vasculitis, the disease may exist for considerable periods without producing hemorrhages. One of us (M. J. H.) has examined a 34-year-old jet pilot who was found to have abnormal retinal vessels during a routine examination four years previously. This patient had never had any symptoms during this period, and examinations had revealed a normal visual acuity. Fundus examination showed typical perivascular venus sheathing with telangiectasia and neovascularization in the upper and temporal quadrants of both eyes.

Secondary Retinal Vasculitis.—Three of the cases were classified as the secondary form of this disease. In all three of these cases iridocyclitis developed initially. One case had Koeppe nodules and large mutton-fat keratitic precipitates. Another was characterized by extensive posterior synechiae and cells and flare in the anterior chamber. The fundi of this patient showed an unusual neovascularization, more extensive around the posterior pole.

Follow-up studies were possible in two of the cases, and both patients showed a progression of the disease. The anterior uveitis has persisted and the visual prognosis appeared to be worse in this group because both the anterior and the posterior segments of the eye were affected.

Postchoroiditis Retinal Vasculitis.—There were three cases of vitreous hemorrhage which were undoubtedly due to vascular erosion by a focus of acute chorioretinitis. Ophthalmoscopic examination when the fundus was visible revealed healed chorioretinal lesions adjacent to the retinal vessel showing perivascular sheathing. The retinal vessels of the rest of the fundus were normal.

Follow-up studies were possible in all three of these cases, and two had 20/20 vision in the affected eye. The third patient had two severe recurrences of bleeding, and the visual acuity was limited to hand movements.

Conclusions

A thorough review of the literature fails to reveal any significant agreement on the etiologic cause of retinal vasculitis.

The results of our preliminary studies show that the hemorrhage is not due to a defect in the hemostatic mechanism.

A study of 21 cases shows that retinal vasculitis can be classified into three categories: (1) primary, (2) secondary, and (3) postchoroiditic. This classification is helpful in evaluating the disease clinically as well as determining the

prognosis. In our small series it appeared that the secondary form of this disease had a worse prognosis than the primary type. However, longer follow-up studies of a larger series is necessary to evaluate this statement.

Pathologic study of 19 eyes revealed that they fall into two groups: (1) primary vasculitis; (2) secondary vasculitis. The first group showed that the initial change was in the vessels; the second group demonstrated an associated uveitis with the vasculitis. Pathological examination showed no evidence of a tuberculous lesion, and no acid-fast organisms were found in any of the suspicious areas of inflammation.

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Observations on Herpetic Keratitis and Keratoconjunctivitis

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Herpetic keratitis has always been a major problem. In 1936 Gundersen [1] wrote that in New England dendritic keratitis was the most frequent corneal infection recognizable on an etiologic or morphologic basis. In 42 months he found it in 221 patients at the Massachusetts Eye and Ear Infirmary. During the same period there were 97 cases of serpent ulcer, 52 cases of phlyctenular keratitis, and 184 cases of interstitial keratitis. This experience was paralleled in most parts of the United States in the prewar years. During the war the disease was extremely troublesome, constituting, in our experience, the major military corneal problem. Since the war it has become an even more serious source of disability; not only are there relatively more cases but they seem also to have increased in severity and in the frequency with which both eyes become involved.

The following analysis of 200 cases of herpetic keratitis and keratoconjunctivitis is part of a broad research program on keratitis* now under way at our medical center as a cooperative effort of the Departments of Microbiology and Ophthalmology and the Francis I. Proctor Foundation for Research in Ophthalmology.

Characteristics of the Series

The 200 cases of the series were drawn from the following three sources: (1) cases seen in the University outpatient clinic, (2) cases referred to the keratitis research unit for etiologic study, and (3) cases seen in our private practices. Although many of the cases referred for consultation could be observed on one occasion only, there were others, particularly in our private practices, that were available for study over a considerable period of time. There were thus an important number in which we were able to observe the evolution of the lesions from their earliest stages to healing. The character of the series, however, prevented the gathering of reliable figures on the long-term visual ravages of the disease. The cases seen in the outpatient clinic and in private practice were unselected, but those referred to the keratitis unit for special study tended inevitably to be unusually severe or complicated cases.

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Diagnosis of Herpetic Keratitis and Keratoconjunctivitis

As a preface to the discussion of the clinical characteristics of herpetic disease in this series, a consideration of diagnostic methods seems in order.

Clinical Diagnosis.—Of first importance in clinical diagnosis is the appearance of the lesion. The disease in its dendritic form is one of the most characteristic clinical entities in ophthalmology. It is generally agreed that keratitis with a typical dendritic figure is invariably due to herpes simplex virus, and certainly none of us has ever seen a typical dendritic figure in herpes zoster or in any other type of corneal disease unrelated to herpes simplex. It is only in the very earliest stages of the formation of the dendritic figure that any confusion in diagnosis could arise. Some forms of nonherpetic epithelial keratitis develop linear lesions without branching which must be differentiated from early dendritic keratitis, but observation of such cases for a few days has in our experience always served to clear up any diagnostic uncertainty.

There are certain variations of the dendritic figure that seem to us to be equally diagnostic. The best example is the so-called "geographic" or "geographic map" ulcer, which has been so named because its irregular outline resembles the map of a continent. It could also be called an "ameboid ulcer" by virtue of the ameboid processes which differentiate it sharply from the ordinary bacterial or traumatic corneal ulcer. Accompanying the typical dendritic figure and the geographic map ulcer, or sometimes preceding their appearance, other epithelial lesions have occasionally been seen, some of them stellate or punctate in form and some filamentary. The stellate lesions when studied under high magnification are seen to be minute dendritic figures and are thus highly diagnostic. Lesions comparable to the punctate and filamentary forms, on the other hand, also occur in nonherpetic keratitis.

The stromal form of herpetic keratitis also has a characteristic appearance. The lesion is disciform, and only rarely is a disciform corneal ulcer nonherpetic. During the period of this study we saw only one case of disciform keratitis that was unrelated to herpes simplex. In this one instance the lesion was caused by herpes zoster virus, but in the past we have also observed it as a feature of accidental vaccinia virus keratitis. It is always a viral reaction and, we believe, can safely be said to indicate herpes simplex virus activity in the vast majority of cases.

In recurrent cases the finding of dendriform or irregularly shaped scars can be a valuable diagnostic aid.

The second most important diagnostic feature of herpetic keratitis, and in our opinion essential to diagnosis, is the loss of corneal sensation associated with the infection. In this series there was not a single case of active herpetic keratitis in which corneal sensation was normal; it was invariably somewhat diminished and in most instances very markedly so. Only in herpes zoster ophthalmicus and neuroparalytic keratitis have we seen a comparable loss of corneal sensation, and neither of these conditions offers any problem in the differential diagnosis of herpes simplex virus keratitis. Associated with this loss in corneal sensation has been a striking lack of photophobia. The only cases with important photophobia have been those with severe secondary iridocyclitis. Most patients have not complained of pain, have kept the affected eye wide open, and have exhibited little or no photophobia when examined with the biomicroscope.

A third feature of herpetic keratitis that has diagnostic value is its frequent association with herpetic lesions of the eyelids, face, and lips. This association

suggests strongly, of course, that the ocular lesions are also herpetic. About one-third of our cases have had such associated lesions.

We found also that the patient's history had definite diagnostic value in herpetic keratitis. Very often a history of previous keratitis in the same eye, often associated with herpes labialis or herpetic vesicles on the eyelids, was elicited. When these recurrences had been precipitated by fever, sunburn, nervous tension, or any other of the well-known herpes-activating mechanisms, it seemed legitimate to suspect that the keratitis was herpetic.

The definitive diagnosis of keratoconjunctivitis as a primary herpes simplex infection can be made by serologic tests only. If the patient's serum shows a rising titer of neutralizing antibody to herpes simplex virus during the active and convalescent stages of the disease, the diagnosis of primary infection is established. It can be strongly suspected, however, in a young child who develops an acute follicular conjunctivitis with fever and preauricular adenopathy, associated ultimately with dendritic figures on the cornea. Usually one of the parents of such a child gives a history of an attack of herpes labialis a few days before the onset of the disease in the infant. We feel that any acute follicular conjunctivitis in a child, with preauricular adenopathy and corneal lesions, should be suspected of being due to herpes simplex virus and that if dendritic figures appear on the cornea a tentative diagnosis of primary herpetic keratoconjunctivitis can be made. We have seen conjunctival hyperemia, sometimes marked, in secondary herpetic keratitis but never a follicular or infiltrative conjunctivitis. We have also seen rare cases of epidemic keratoconjunctivitis in infants and young children which have resembled primary herpetic keratoconjunctivitis in the type of conjunctival reaction, but in these the differential diagnosis has never been difficult to make, because of the differences in the corneal lesions.

Laboratory Diagnosis.—Virus Isolation: From the time of Grüter[2] the laboratory diagnosis of herpetic keratitis has been made by the inoculation of the rabbit cornea with scrapings from the corneal lesions. In his excellent study in 1936, Gundersen used this method exclusively. It has the distinct advantage that the rabbit develops a characteristic disease with typical dendritic figures. No other experimental disease of the rabbit cornea develops these figures, and only in experimental vaccinial infection is there a keratoconjunctivitis that resembles herpetic disease in any important way. The two experimental diseases are readily differentiable, moreover, since the cytoplasmic inclusion body of vaccinia is easy to demonstrate in epithelial scrapings stained by Giemsa's stain or other cytologic stain. Inoculation of the rabbit cornea may thus be regarded as a satisfactory means of identifying herpes simplex virus infection.

Recently, however, other methods have come into use. These include mouse brain inoculation, inoculation of the chorioallantoic membrane of the developing chick embryo, and tissue culture. The mouse has the advantage of being an inexpensive animal, but the induced encephalitis is not pathognomonic of herpetic disease and the virus must be certainly identified by means of neutralization tests. The chorioallantoic membrane is also cheap and has the advantage of being more susceptible to herpes simplex virus than the rabbit cornea. The small lesions produced by it can be differentiated readily from those produced by vaccinia virus, and so their production can also be considered a good presumptive test of herpes simplex infection. Unfortunately, however, a number of nonspecific lesions can also develop on the chorioallantois and are a source of confusion. Certain iden-

tification of the virus can, again, be made only by means of time-consuming neutralization tests.

Currently we are using tissue culture of HeLa carcinoma cells for the diagnosis of herpetic keratitis. This is a low-cost method, and its sensitivity with respect to herpes simplex infection seems to parallel that of the chorioallantoic membrane. The presence of the virus can be presumed on the basis of its cytopathogenic effect and sometimes also on the demonstration of intranuclear inclusions. For certain identification, however, neutralization tests must be performed.

In the present study we found that herpes simplex virus could be isolated consistently only from early dendritic lesions. Scrapings of corneal epithelial cells were found to be much more reliable for inoculation purposes than conjunctival washings. It was usually impossible to isolate the virus from disciform keratitis even when typical dendritic figures had preceded the stromal involvement. We should like to emphasize that the diagnosis of herpetic keratitis remains essentially a clinical diagnosis and that laboratory findings are for the most part confirmatory only.

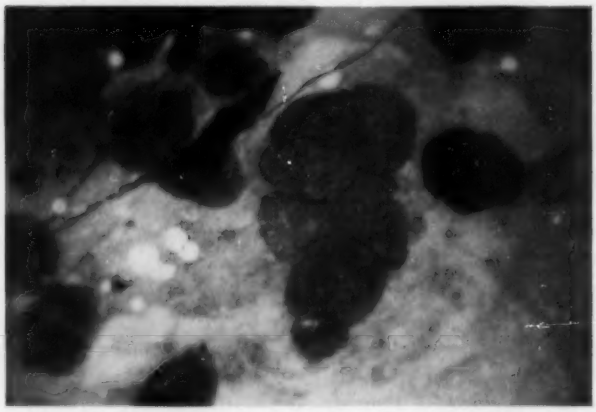

Fig. 1.—Multinucleated giant epithelial cell in corneal scrapings from a case of dendritic keratitis. Giemsa stain; reduced from mag. × 800.

Cytologic Diagnosis: The diagnostic value of epithelial-cell changes in herpes simplex infections has been emphasized by Tzank[3] and more recently by Blank and associates.[4] In scrapings from herpetic vesicles, these observers noted giant epithelial cells with eight or more nuclei. Normal chromatin granules and nucleoli were absent. The nuclei, stained by Giemsa stain, were filled with red-violet stringy amorphous material, while the cytoplasm stained blue and frequently contained green melanin granules. All stages in the transformation of these giant cells from cells with single large nuclei were observed. Blank and his coworkers noted identical cell changes in vesicular material from herpes zoster and varicella but failed to find them in material from many other diseases studied. Since varicella and zoster are clinically distinct from herpes simplex, it seemed to us that if this cytologic picture could be found regularly in corneal scrapings from herpetic keratitis, it would have unique diagnostic significance.

Accordingly, we studied a large number of scrapings from dendritic ulcers and a limited number of scrapings from other types of herpetic keratitis. Multinucleated epithelial cells (Fig. 1) were a common finding, but they were not as large, nor did they contain as many nuclei, as those that Blank and associates reported finding in scrapings from skin lesions and which we also were able to

see in scrapings from herpetic vesicles of the eyelids. We felt, nevertheless, that the presence of multinucleated giant epithelial cells could be considered strongly suggestive of herpes simplex infection.

We were unable to demonstrate intranuclear inclusions in scrapings from any of our cases or in scrapings from the experimental disease in rabbits; we had no difficulty demonstrating them in sections of the rabbit cornea, however. In the cases of acute follicular conjunctivitis in children, which we believe represented the primary form of the disease, we found the characteristic viral reaction: a scanty exudate containing a predominance of mononuclear cells, chiefly lymphocytes and monocytes. No inclusions were found in the conjunctival cells in these scrapings, but there were a few multinucleated epithelial cells. We intend to look for inclusions in biopsy specimens from this type of case in the future.

Serologic Diagnosis: Since over 90% of the population are carriers of herpes simplex virus,[5] and high neutralizing antibody titers can be demonstrated in their sera, it is obvious that serologic findings can be expected to have only negative value in the diagnosis of the common, secondary types of herpetic keratitis. On the other hand, definite diagnosis of the primary form of herpetic keratoconjunctivitis rests solely on the demonstration of a rising titer of neutralizing antibody to the virus during the course of the disease. As noted above, however, it is our belief that a presumptive clinical diagnosis can legitimately be based on the association of an acute follicular conjunctivitis with preauricular adenopathy and dendritic figures on the cornea.

A more detailed discussion of the laboratory aspects of the diagnosis of herpetic ocular disease as encountered in this series will be presented by our group in a subsequent paper.

Clinical Forms of Herpetic Keratitis and Keratoconjunctivitis: Analysis of 200 Cases (Table)

	Cases ,No.	
Primary form: acute keratoconjunctivitis		9
Secondary forms: superficial or deep keratitis		191
A. Superficial forms	132	
1. Dendritic keratitis and allied lesions (punctate, stellate, filamentary)	98	
2. Geographic map keratitis	34	
B. Deep forms	59	
1. Disciform keratitis (with or without bullous keratitis and ulceration)	57	
2. Hypopyon ulcer	2	

Primary Herpetic Keratoconjunctivitis

In the present series we observed nine cases, all but one of them in children, which we believe in each case represented the patient's initial attack of herpetic disease. Unfortunately it was possible in only one of these (a young adult) to prove the point serologically. The other cases were seen in consultation, and convalescent sera could not be obtained from them.

All nine cases were characterized by acute follicular conjunctivitis with preauricular adenopathy and associated epithelial keratitis, and in every case dendritic figures appeared during the course of the disease. In five of the nine cases there were concomitant herpetic lesions of the eyelids and face, and in two there was concomitant herpetic stomatitis. No pseudomembranes were seen, although

they have been described as occurring occasionally in this type of case. It was of interest to us that in several instances the dendritic lesions were preceded by a punctate type of epithelial keratitis in which the punctate spots eventually coalesced to form definite figures. We were also impressed by the self-limited nature of the corneal manifestations of this primary form of the disease; in none of the nine cases was it necessary to curette or cauterize the cornea. Spontaneous healing of both conjunctival and corneal lesions in these first attacks seemed indeed to be almost the rule. Recurrences, however, tended to follow the usual pattern. In the young adult case there was a recurrence that was dendritic at onset and then developed into a typical disciform keratitis.

We were impressed by the severity of the conjunctival changes and by the resemblance of the disease in its initial stages to epidemic keratoconjunctivitis. Differentiation was simple, however, as soon as the corneal lesions became fully developed. The obvious source of infection in the family was interesting: In seven of our nine cases the mother or father, or both, had active herpes labialis preceding the onset of the child's infection by several days.

Superficial Forms of Herpetic Keratitis

Dendritic Keratitis.—In 132 of our 200 cases the lesions when first examined were superficial, and dendritic figures were seen in 98 of the 132. Roughly half of our cases could thus be designated as dendritic keratitis. The dendritic figures varied greatly in size, number, and location. They involved all quadrants of the cornea but seemed to have a definite propensity for the pupillary area. The figures in six cases were strictly marginal, but the great majority involved the pupillary area to a greater or less extent. Extremes of involvement varied from a single dendritic figure extending entirely across the cornea through the pupillary area to multiple tiny dendritic figures, each of them star-like in appearance and constituting together the so-called "stellate keratitis." As many as 15 distinct figures could be counted in one of our cases. Along with the dendritic figures, a number of atypical epithelial lesions were seen, usually punctate in character but occasionally filamentous. One case in particular showed many filaments along with dendritic figures. We never have seen a pure filamentary keratitis as a form of herpetic disease, but on a number of occasions we have noted a scattering of filaments along with the other corneal lesions of herpes.

Geographic Map Keratitis.—The second characteristic form of superficial

Fig. 2.—"Geographic" type of herpetic corneal ulcer, showing the diagnostic ameboid processes.

herpetic keratitis is the so-called "geographic" or "geographic map" ulcer (Fig. 2), which we have discussed above in connection with diagnosis. There were 34 examples of this herpetic lesion among the 200 cases of our series. It appears to us to represent an expanded form of the dendritic figure, its ameboid processes giving it an appearance totally unlike that of any of the bacterial forms of central ulcer. In a number of instances we were able to follow its development from a dendritic ulcer. It was never seen as the initial lesion of herpetic disease but only in cases that had been active for some weeks. It was particularly characteristic of the cases that had had prolonged topical cortisone therapy.

In general, the geographic ulcer appeared to involve the stroma more deeply than the usual dendritic ulcer, and it was our impression that the subsequent scars were much denser than those left by the typical dendritic figure. Like the dendritic ulcer, the geographic lesion seemed to have a special predilection for the pupillary area. But, although we have known a few cases of dendritic keratitis to heal spontaneously, there was in this series no single instance of such healing of a geographic ulcer.

In addition to these two commonest forms of superficial keratitis, the dendritic and the geographic, we have also encountered a few round epithelial ulcers in totally anesthetic corneas in cases that had suffered repeated attacks of herpetic keratitis. These we have regarded as trophic rather than herpetic lesions. We have purposely avoided the term "metaherpetic keratitis," which has been used variously to describe the sluggish ulcers (Gundersen[1]) we believe to be trophic and the stromal lesions (Braley[6]) for which the term "disciform keratitis" seems to us to be quite satisfactory.

Deep Forms of Herpetic Keratitis

Disciform Keratitis.—There were 59 cases of deep stromal involvement in this series. Fifty-seven of them were classified as disciform keratitis, and two additional cases passed through a disciform stage but are described below as cases of hypopyon ulcer.

Many of these disciform cases (Fig. 3) were known to have followed dendritic keratitis which had failed to respond to therapy, particularly to therapy with the steroid hormones. There were a few in which no initial dendritic figure was recognized; their herpetic nature, however, could be presumed on the basis of other clinical evidence, e.g., the presence of dendriform scars, a loss in corneal sensation, or associated herpetic lesions of the skin or lips.

Fig. 3.—Subsiding herpetic disciform keratitis which followed an initial dendritic lesion.

There was a marked variation in the severity of the disciform cases. In the mildest forms the stroma was edematous and there was minimal cellular infiltration and new-vessel formation. In the cases of this type that we were able to follow, the final visual result was usually good and cicatrization was minimal. At the other extreme were a number of severe cases in which there was a heavy infiltration of the corneal stroma and extensive new-vessel formation and in which bullous keratitis with ulceration developed, probably as a result of endothelial damage. It was this type that was often associated with severe uveitis. In many instances, though not invariably, these severe forms of stromal herpetic keratitis had been under treatment with cortisone or one of the related steroid hormones.

Hypopyon Ulcer.—Among these deep forms of herpetic keratitis there were two cases of hypopyon ulcer, both of which resulted in loss of the globe and in both of which the herpetic disease had progressed from typical dendritic figures through disciform keratitis to deep ulceration. Secondary invaders were found in both cases, in one a bacterium of the Hemophilus group and in the other a fungus, Candida albicans. Apart from this series we have seen several cases of hypopyon ulcer following dendritic keratitis in which no secondary invaders could be demonstrated and which we feel were due to herpes simplex virus alone. In the two cases in this series we feel that the prolonged use of steroid hormones was probably a factor in the development of the ulcers.

In the literature [7] there are a number of references to "herpetic interstitial keratitis." We have not applied this term to any of our cases, but some of them progressed to total involvement of the corneal stroma and could thus have legitimately been called "interstitial." There were no cases, however, which could have been confused with a syphilitic or tuberculous type of interstitial keratitis.

Perforation of the cornea occurred in three of our cases; two were the cases with hypopyon ulcer and one was a case in which central necrosis of the stroma occurred in the course of a severe disciform keratitis. Outside this series we have seen, or have been informed of, five additional cases of perforation of the cornea, all of which were apparently associated with the prolonged use of the steroid hormones. It is noteworthy that prior to the use of steroids we had seen or heard of only one case of perforation in herpetic keratitis.

In this series we had no instance of generalized herpetic disease associated with the keratitis. In a previous observation period, however, we observed two cases of the so-called "Kaposi varicelliform eruption." This clinical entity, which may be very severe and carries a definite mortality rate, is seen principally in children with atopic eczema. It is of interest that in nine cases of the present series there was associated atopic eczema but that in none of them did the generalized eruption supervene.

Bilateral Cases

Nineteen of our two hundred cases were bilateral. Prior to World War II bilateral cases were extremely rare. Gundersen [1] had only one bilateral case in his series, and in this prewar period only one of us (P. T.) had ever observed a case. This was a single case in an infant. Since the war we have all seen an appreciable number of bilateral cases in addition to the 19 included in the series. In our opinion, this represents a rather startling change in the character of the disease. Two of our nineteen bilateral cases followed the use of hydrocortisone

for the treatment of allergic dermatitis of the lids and associated allergic conjunctivitis.

Trigger Mechanisms in Herpetic Keratitis

One of the most characteristic features of herpetic disease of the skin and mucous membranes is the trigger mechanism by which fever induces a recurrence. This is seen characteristically in patients with pneumonia, more than 50% of whom can be expected to come down with herpes labialis. Fever is certainly also the commonest trigger mechanism in recurrent herpetic keratitis. In our series of 200 cases there were 61 that followed fever from various causes, including smallpox vaccination in 2 instances and tetanus immunization in 1. There were 20 cases that followed trauma and 5 that followed exposure to chemical irritants. Sunburn was apparently the exciting agent in four cases, and emotional crisis in six. It was of special interest to us that seven cases followed the use of hydrocortisone topically; one followed the use of prednisolone (Meticortelone), and one, the use of cortisone. There was no trigger mechanism, or none that could be elicited from the history, in 94 cases. This is in contrast to herpes labialis, in which a trigger mechanism can be identified almost invariably.

Role of Secondary Bacterial and Mycological Infection

Secondary bacterial infection was rare in our series. In a few instances we found Staphylococcus aureus infection of herpes simplex vesicles of the eyelids. Except for the two cases of hypopyon ulcer, however, secondary infection did not appear to play any part in the clinical course of our cases of herpetic keratitis.

Distribution of Cases According to Number of Attacks

Of our 200 cases, 120 were seen at the time of the first attack and 38 at the time of the second. The remainder had had from two to seven previous attacks, and 16 patients stated that they had had innumerable attacks. Of the latter, two were middle-aged patients whose initial attacks had occurred in childhood. We had one patient, a middle-aged woman, who had had her initial herpetic ocular infection at the age of 4 and since then had had from 5 to 10 attacks yearly. In her case there appeared to be multiple trigger mechanisms, including fever, menstruation, and emotional upsets. This patient received a lamellar type of corneal graft as a therapeutic measure and has been free of herpetic attacks ever since. The use of keratoplasty in this type of case will be discussed later in the section on therapy.

Although it is the rule for herpes labialis to keep recurring throughout life, we have observed over the years, apart from this series, a number of patients known to have had only a single corneal attack with no recurrence of any kind for many years.

Distribution of Cases According to Age and Sex

As has been found consistently in other series, males were affected more commonly than females; 135 of our patients were males, and 65 were females. Unlike the series reported by Gundersen in 1936, in which the highest incidence of the disease was in children, the majority of our cases were between 21 and 60 years of age. Only nine were under 5. Twenty-one were over 60, and there was one patient in whom the initial ocular attack occurred at age 83. In this

respect our experience coincides with what we found while in military service, i. e., that there was a high incidence of herpetic disease in the military age group.

Visual Loss from Herpetic Keratitis

Since the majority of our cases were referred to us for consultation, and so could not be followed over any considerable period, it was impossible to make a statistical analysis of visual loss for the series as a whole. We are able to say, however, that major temporary diminution of vision was the rule, and we feel that permanent diminution of vision probably obtained in the majority of cases because of the almost invariable involvement of the pupillary area. The globes were lost in three cases, and in an appreciable number of the disciform cases vision was reduced to light perception only. On the other hand, we were struck by the fact that, in a considerable number of dendritic cases with pupillary involvement, vision temporarily diminished gradually returned over a period of months or years. Unfortunately, recurrent attacks tended to neutralize such improvement and we must conclude that in our experience herpetic keratitis in the United States leads to more reduced vision than any other corneal disease.

We were impressed by the great economic cost of this disease, that is apparent not only in the lost or diminished vision known to have been caused by it but in the work-time lost during the all too frequently recurring attacks. A number of our patients have been unable to hold steady jobs because of the frequency of the recurrences.

Medicolegal Aspects of Herpetic Keratitis

In this series industrial connection was claimed by a considerable number of patients, often only on the basis of foreign-body sensation preceding the onset of the keratitis. There were 20 cases, however, which developed two or three days after definite trauma. It seemed to us reasonable to suppose that the trauma had been the exciting agent in these cases, since it is well known from studies on the rabbit cornea that trauma facilitates herpetic infection. In the five cases which followed exposure to chemical irritants of various sorts, the time relationships also suggested strongly that these exposures had excited the herpetic attacks.

In our opinion industrial connection should be allowed only in cases in which proved trauma or foreign body preceded the onset of the keratitis by the several days corresponding to the incubation period of the disease. The claim of a foreign body sensation in the eye, without proof of the existence of a foreign body, should not, in our opinion, be regarded as evidence of industrial relationship.

Observations on Epidemiology

Only in the few primary cases was any information available on the probable source of infection. In seven of the nine primary cases there was a typical history of fever blisters in the mother or father preceding by several days the onset of the acute keratoconjunctivitis in the child. In other cases seen outside the present series we have also been struck by the association between herpes labialis in the parents and the acute keratoconjunctivitis or stomatitis in the child.

We have noted an apparent occupational relationship between herpes keratitis and the practice of dentistry. Over the years we have observed a high incidence of the disease among dentists, and in the present series there were three. Even this seems a noteworthy number, since in the same series there were no cases

among physicians, a comparably numerous professional group. It is known that herpes virus can be isolated from the mouths of apparently normal persons, and so the exposure of dentists, who are cleaning and otherwise treating teeth, might very well be high. For this reason we have occasionally prescribed glasses for dentists in the absence of significant refractive error.

In one case not included in this series we observed herpetic keratitis in a rhinologist. Pediatricians might be expected to be unduly exposed to herpes simplex virus, but we never have seen an instance of herpetic keratitis in a member of this professional group. Curiously enough, except for one instance in this series, we never have seen herpetic keratitis among railroad men, in spite of the frequency with which they must inevitably have foreign bodies removed from their corneas.

Therapy of Herpetic Keratitis

The tendency of the primary type of herpetic keratitis to heal spontaneously has already been noted. Spontaneous healing has also been observed occasionally in secondary forms of the disease, particularly in disciform keratitis. We would estimate, however, that spontaneous clearing of herpetic keratitis within a reasonable period of time does not occur in more than 10% of cases.

In spite of early hopes that the broad-spectrum antibiotics would influence the disease favorably, it is our experience that the sulfonamides, antibiotics, and other chemotherapeutic agents can now be said to have no appreciable effect on herpetic keratitis. In the small series of cases in which we tried repeated smallpox vaccinations in an attempt to prevent herpetic relapses, the results were negative. In this connection it seemed of more than passing interest that one of our cases followed smallpox vaccination, which apparently acted as a trigger mechanism, probably by inducing fever. In our opinion the only treatment of value in this disease consists in the destruction of the virus in the epithelial cells by curettage or chemical cauterization, and this method is useful only in the superficial forms of the disease. The removal of epithelium is not only of no value in disciform lesions but may actually be harmful.

When cortisone was first introduced for topical use, we immediately tested it in a number of cases of dendritic and other forms of herpetic keratitis. The anti-inflammatory effect of the medication was apparent, and most patients experienced a relief from symptoms. This was particularly striking in the disciform cases complicated by secondary iridocyclitis. It soon became clear, however, that the steroid effect was actually a masking effect and that the end-results in cases so treated were inferior to the results in cases not treated with steroids. Thus, although we have had four dendritic cases in which cortisone appeared to be useful in reducing inflammatory signs and in effecting remissions, on the other side of the ledger we have a number of cases in which we feel that cortisone therapy either contributed to or induced stromal necrosis. This clinical impression has been definitely substantiated by the results of experiments on herpetic keratitis in rabbits performed by us and by a number of other observers. One of us (S. J. K.) will soon report on an extensive experimental study of steroids in experimental herpetic keratitis in which cortisone and the related newer steroids were employed.

In addition to the unfavorable effects we have noted from the use of steroids in the treatment of herpes simplex keratitis, we have had the experience of seeing herpetic keratitis actually develop under steroid therapy. Hydrocortisone,

particularly, seems to have had a precipitating effect on the disease. As previously noted, we have had two cases of bilateral dendritic keratitis which occurred while the patients were being treated with hydrocortisone for allergic conjunctivitis and dermatitis of the eyelids. In neither patient was there a previous history of herpetic keratitis. In analyzing our present series of 200 cases we noted that the worst cases had all received cortisone or other steroids, some for prolonged periods. Both cases of hypopyon ulcer, which resulted in perforation and loss of the globe, had had prolonged and extensive topical steroid therapy. In view of these unhappy experiences, we feel that cortisone and the related steroids should not be used in the treatment of herpetic keratitis in spite of the anti-inflammatory effect and in spite of the marked symptomatic relief usually experienced.

Since many cases of herpetic keratitis have recurrent attacks induced by definite trigger mechanisms, we have tried to forestall or interrupt several of these mechanisms in an effort to prevent relapses. In the still small series of cases in which fever induced by respiratory infections appeared to be the exciting agent, we have provided the patients with a combination of acetylsalicylic acid compound and chlorpheniramine (Chlor-Trimeton) so as to reduce the febrile and allergic manifestations of the infections. In studying the patterns of recurrence in these cases it seems to us that this method of treatment has been of some value. In cases apparently triggered by sunburn we have provided the patients with sunglasses and head coverings and have urged avoidance of excessive exposure. And in the few patients we have seen in whom an emotional crisis has seemed to be the trigger mechanism, we have recommended that a tranquilizing agent be immediately available to tide the patient over the episode. We have also urged the avoidance of systemic or topical steroid therapy for patients known to have recurrent herpetic keratitis. A parallel control series is being left untreated, and we expect to report our findings later when a series large enough to permit analysis will have accumulated.

Corneal Transplantation in the Treatment and Prophylaxis of Herpetic Keratitis.—Various types of keratoplasty for patients with active herpetic ulcers and inactive scars affecting vision have been advocated for a number of years. Lamellar keratoplasty has been recommended for cases with superficial scars or with frequently recurring dendritic ulcers; full-thickness grafts have been recommended for cases with deep scars. According to Franceschetti,† lamellar keratoplasty has proved particularly helpful to patients who have been unable to hold steady jobs because of constant recurrences.

In our series, 16 patients with herpetic keratitis were subjected to a total of 20 keratoplastic operations. Of these, 18 were full-thickness grafts and 2 were lamellar. The 16 patients could be divided into the following groups: (1) those with healed herpetic corneal scars; (2) those with chronic persistent deep ulcers, and (3) those subject to repeated attacks of herpetic keratitis.

The results were most satisfactory in the first group, with healed lesions, since it was possible in these cases to bring the graft into contact with a large area of normal cornea. In the second group, with deep chronic ulcers, the surgery was undertaken with the understanding that it was for the purpose of saving the eye and that the possibility of improving vision was remote. The unfavorable aspect of keratoplasty in this type of case lies in the fact that the graft comes

† Franceschetti, A.: Personal communication to the authors.

into contact with inflamed corneal lamellae and that sutures are placed in edematous and somewhat pliable tissue. In view of the marked peripheral corneal opacification which these patients exhibit, and the frequent occurrence of anterior synechiae, we have felt it desirable to excise all of the pupillary portion of the iris at the time of surgery. For the third group of patients, composed of those with repeated recurrences, and for those patients in the first group with superficial scars only, lamellar keratoplasty has been a satisfactory procedure.

In none of our patients, some of whom were operated on as long as five years ago, has there been a recurrence of herpes in the eye operated on. It is interesting that some of them were treated with hydrocortisone in the postoperative period without experiencing a herpetic relapse.

Comment

There seems to be no adequate explanation for the apparent increase in the incidence and severity of herpetic keratitis in the postwar period. It has been suggested that the increase is more apparent than real, that the seriousness of the herpetic problem has simply been accentuated by the decrease in the incidence of bacterial keratitis resulting from the use of sulfonamides and antibiotics. Although our data on this point are insufficient for statistical analysis, we feel sure that a real change has taken place, and we offer as evidence our 19 cases of bilateral herpetic keratitis, 2 of which were apparently induced by hydrocortisone therapy. We think there is general agreement that bilateral cases were extremely rare in the prewar period. Most ophthalmologists whom we have consulted have stated that they never saw a bilateral case until after the war.

Another explanation that has been offered is that the drop in the normal bacterial flora of the eye through the frequent use of antibiotics and sulfonamides has served to potentiate the viruses in a way comparable to the potentiation of Monilia in the intestinal tract when broad-spectrum antibiotics have reduced the bacterial flora. We doubt if this could be the case in the eye, since the bacterial flora of the normal eye is scanty and bears no resemblance to the abundant flora of the intestinal tract.

In reviewing our 200 cases we noted the relative ease with which herpetic keratitis could be differentiated from other types of keratitis by means of clinical examination. This is true even in the nondendritic and late, recurrent forms of the disease. Our over-all feeling is that the clinical picture of herpetic keratitis is highly characteristic. The reliability of the clinical diagnosis does not entirely eliminate the need for laboratory studies, however, at least in some of the atypical cases. The laboratory procedures unfortunately cannot yet be used reliably and cheaply by the average ophthalmologist, nor are adequately equipped laboratories available as yet in all the large centers. There is a very real need for a simple diagnostic method by which the virus could be recognized under the ordinary light microscope. If it were possible to identify the inclusion bodies in corneal scrapings from the disease, as may be done in vaccinial keratitis, molluscum contagiosum, and trachoma, the problem would be solved. For, in spite of the fact that the intranuclear inclusions of this disease are not pathognomonic, the possibility of infection of the cornea with any other virus producing similar inclusions is so remote that to demonstrate this type of inclusion would be tantamount to isolating the virus.

The recurrent nature of herpetic keratitis and the trigger mechanisms which

set off the recurrences are characteristics all but limited to this type of corneal disease. Only phlyctenular keratitis has any comparable sort of mechanism. If it were regularly possible to remove or modify these trigger mechanisms, it would seem that the recurrences might be prevented.

Most unhappily, the therapy of herpetic keratitis has not progressed in the last few years and, in fact, the introduction of cortisone and the related steroids has actually caused it to regress. In our series almost every one of the patients referred to us for study had received cortisone therapy in spite of the fact that much had already been written [8] on the unfavorable effect of these preparations on the disease. There is no doubt in our minds that the use of the steroid hormones has been responsible in part for the perforations and sluggish corneal ulcers so characteristic of herpetic keratitis in this postwar period. We feel that the only advance in therapy has been in the field of keratoplasty and that this approach is not widely applicable.

Summary

A series of 200 cases of herpetic keratitis and keratoconjunctivitis have been analyzed according to diagnostic methods, clinical characteristics, trigger mechanisms, visual loss, age of onset, number of attacks, and results of therapy. It is concluded that herpetic keratitis is now the most important corneal disease leading to loss in vision in the United States and that further research, oriented particularly toward therapy and prophylaxis, is urgently needed.

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Scoliosis and Vertical Ocular Muscle Imbalance

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The term "ocular torticollis" has existed in the ophthalmologic literature since Cuignet [1] first introduced it in 1873. However, only a few authors * have ever bothered to mention the total spinal disalignment which occurs with vertical ocular muscle imbalance.

In this paper a selected series † of cases will be presented to illustrate the spinal scoliosis that is produced when a vertical muscle weakness is present from birth.

Report of Cases

CASE 1.—A 24-year-old white man presented himself with the history that he had been able to produce double vision when looking to the right for as long as he could remember. He stated that he normally suppressed diplopia but could produce it at will. The patient has no other eye complaints, but he has noted a head tilt to the right for many years. A routine physical examination in March, 1952, revealed a scoliosis of the spine. Past history was noncontributory.

Eye examination:

Visual acuity: 6 meters: O.D. 20/20; O.S. 20/20
50 cm.: O.D. 20/15; O.S. 20/15

Refraction (cycloplegic): O.D. $-50+75\times 70=20/15$
O.S. $-50+75\times 100=20/15$

External examination: Lids, lacrimal apparatus, corneae, conjunctivae, pupillary reaction, tactile tension, irides, and extraocular movements essentially normal, O.U.

Howard-Dolman test: Passed.

Heterophoria (Maddox rod): Distance: EXO 1.5; LH 3
Near: EXO 5; LH 3-4

Near point of convergence: 30-40 mm.

Accommodation: O.D. 12.5; O.S. 12.5

Red lens test: Diplopia at 14 in., right upper diagonal; 12 in., right horizontal; 14 in., right lower diagonal.

Bielschowsky test (head-tilting test): (Upward movement, left eye) positive to left shoulder; downward movement of right eye to left shoulder.

Screen and prism (see Fig. 1).

Screen and cover (see Fig. 1).

Recorded for publication May 4, 1956.

Kresge Eye Institute.

* References 1a-5.

† The cases reported have been selected from a series numbering more than 30. The remainder were deleted because of the over-all similarity of findings.

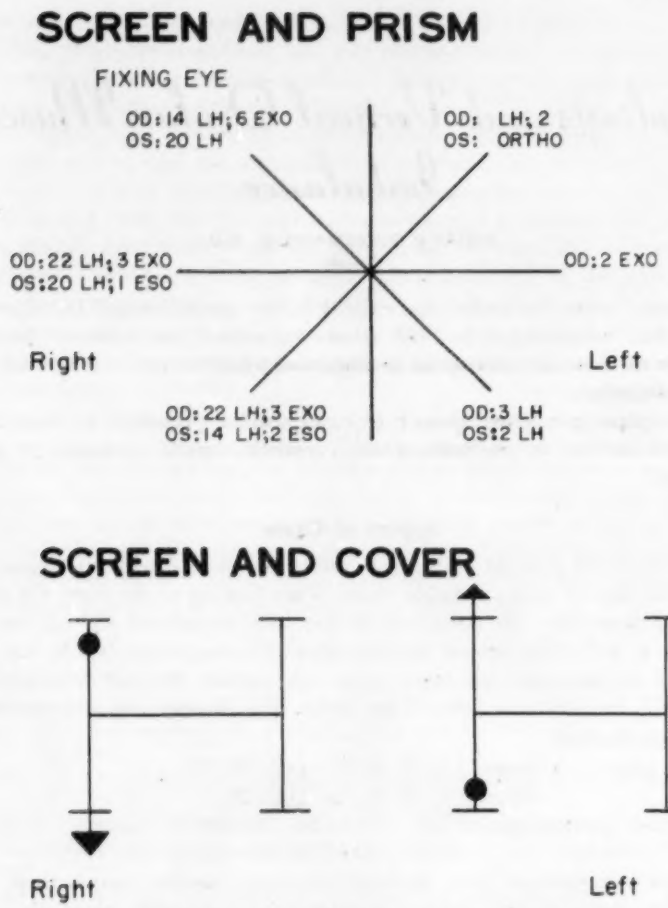


Fig. 1 (Case 1).—The results of the screen and prism reveal right superior rectus and left superior oblique weakness. Diagrammatic results of the screen and cover test bear this out. (Diagrams are made as if looking at the patient.)

Peripheral fields: Full to 3/330 white test objects, O.U.

Slit lamp examination: Corneae, clear; A.R. and K.P. negative; anterior chambers, irides, lenses, and anterior vitreous normal, O.U.

Hruby lens: Posterior retinal segments essentially normal, O.U.

Ophthalmoscopic examination: Mediae clear; discs, maculae, foveal reflexes, and vessels essentially normal, O.U.

Photographs (Figs. 2 and 3): Head tilt to right with face tilt to right. Front and back views of the patient stripped to the waist reveal a shift of the lumbar spine to the right as seen from the back with a compensatory shift of the thoracic spine to the left and the neck to the right with a definite face tilt to the right. There is a definite shortening of the distance from the deltoid process of the scapula to the interscapular spine on the right in countradistinction to the left.

X-ray examination (spine, Fig. 4): "There is a moderate scoliosis of the lumbar spine with convexity to the right. A compensatory scoliosis of moderate

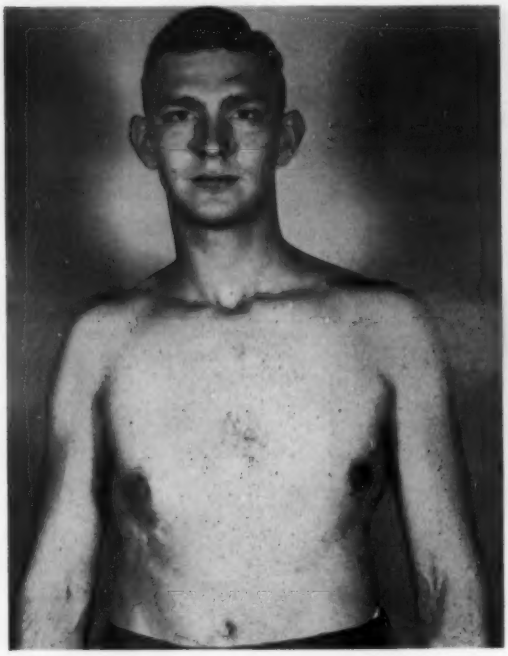


Fig. 2 (Case 1).—Front view. Note head tilt and slight face tilt to right with shift of thoracic spine to left.

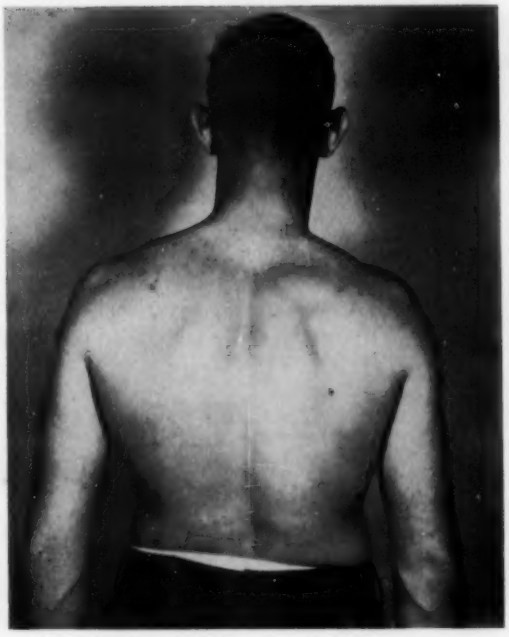


Fig. 3 (Case 1).—Back view. The head tilt to the right is compensated by the thoracic spine shift to the left and lumbar shift to the right.

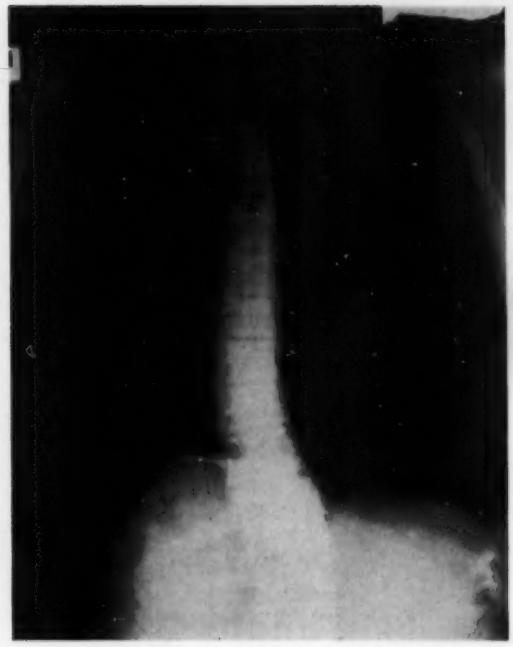


Fig. 4 (Case 1). — X-ray (Bucky) shows the scoliotic deformity of the spine. Actually, there is no abnormality of the bone.

degree is present in the thoracic spine with convexity to the left. No other abnormality is noted in these portions of the spine. In the lateral view the normal lordotic curvature of the cervical spine is absent. Impression: No abnormality can be demonstrated other than scoliosis."

Leg measurements (anterior superior spine to the medial malleolus): Right leg, 39 in.; left leg, 39 in.

Impression.—left superior oblique weakness and inhibitional weakness of contralateral antagonist, right superior rectus.

Case 2.—A 24-year-old white man with history of head tilt and difficulty maintaining binocular single vision as long as he could remember. Diplopia became more and more uncomfortable. Past history noncontributory.

Eye examination: V.R.E. 20/20; V.L.E. 20/25.

External examination: Negative save for protective ptosis, left eye; head tilt to right with right face tilt and chin depression. Thoracic shift to left and lumbar shift to right. Left hypertropia and intermittent exotropia.

Screen and cover (only with left eye fixing):

Ophthalmoscopic examination: Negative, O.U.

Refraction (cycloplegic): R. $+0.12+0.37\times180=20/20$

L. $-0.50+1.25\times\ 70=20/25$

Lancaster red green test revealed a left hypertropia greatest when looking

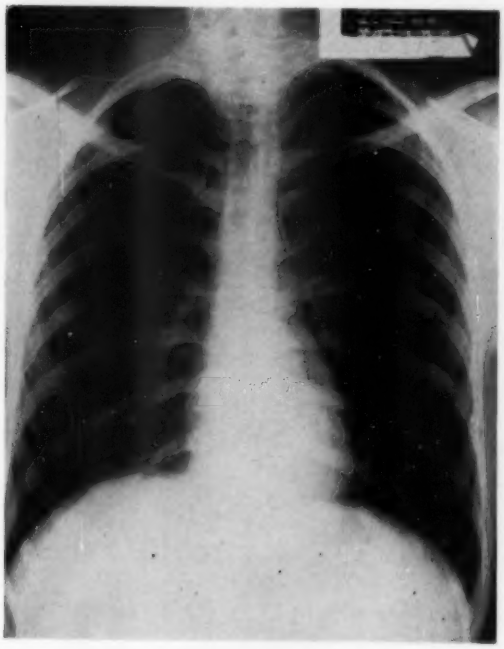


Fig. 5 (Case 2).—Upper spine.

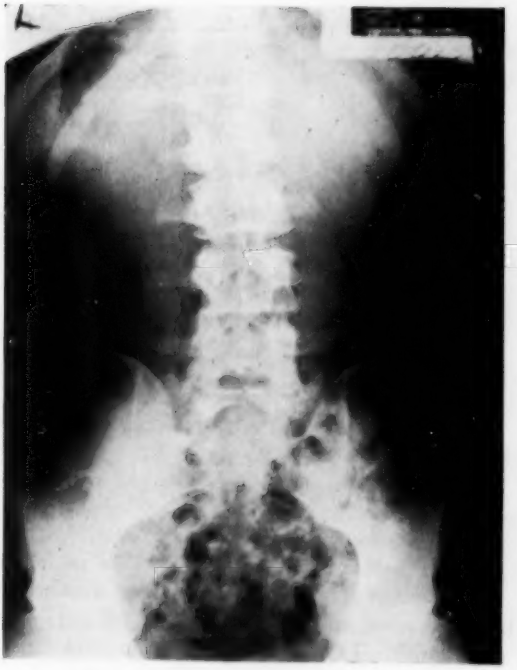


Fig. 6 (Case 2).—Lower spine.

to the right and down, right or left eye fixing. There was diplopia in any position to right.

Bielschowsky test: Positive to left shoulder.

Leg measurements (anterior superior spine to lateral malleolus): Right leg, 37 in.; left leg, 37 in.

X-rays: Scoliosis is to right upper thoracic and lumbar regions (Figs. 5 and 6). No bony abnormalities.

Impression.—Left superior oblique palsy.

Program.—A myomectomy of the left inferior oblique was performed, and by one month postoperatively the patient's ocular status was improved. Diplopia was present only upon looking to the right and down. A marked improvement in head and body posture was noted. Subjective improvement was marked.

Case 3.—A 23-year-old white man with occasional diplopia to the right and no other ocular difficulties. Past history, noncontributory.

Eye examination: V.R.E. 20/20; V.L.E. 20/20.

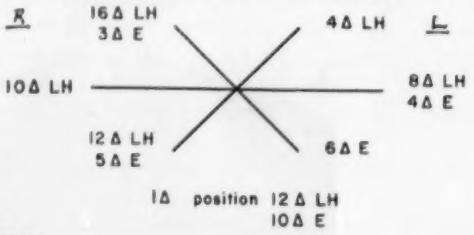
Refraction (cycloplegic): R. +0.50×170
L. +0.50

External examination: Negative except for a head tilt to the right, compensatory thoracic spine shift to left, and lumbar shift to right.

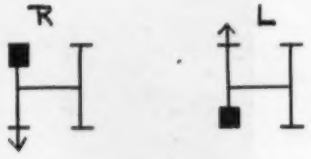
Cover test: diplopia in all fields of gaze when the head is held erect; left hyperphoria and esophoria.

Screen and prism: Distance (without correction): 10 D. esophoria, 4 D. left hyperphoria. Near: 2 D. esophoria, 15 D. left hyperphoria.

Cardinal positions (left eye fixing, head held erect):



Screen and cover:



Stereopsis: Poor.

Bielschowsky test: Positive to left shoulder.

Leg measurements (anterior superior spine to lateral malleolus): right leg, 37 in.; left leg, 37 in.

X-rays: Minimal scoliosis to right upper thoracic with compensatory right scoliosis in lumbar area (Fig. 7).

Ophthalmoscopic examination: Negative, O.U.

Visual fields: Normal to 3/330 white peripheral and 1/1000 white centrally.

Impression.—Left superior oblique weakness with inhibitional palsy of contralateral antagonist (right superior oblique) and esophoria.

Program.—Left inferior oblique myomectomy was performed at the origin,

Fig. 7 (Case 3).—Lower spine. Posteroanterior view.

and the muscle was also recessed at the insertion. One month postoperatively the left hyperphoria was gone for distance. There were 4 D. L.H. for near, and patient had no diplopia in any position of gaze. A slight head tilt persisted.

CASE 4.—A 26-year-old white man. Patient had known of some trouble with diplopia all his life, becoming more evident as he grew older. No other ocular symptoms. Past history, noncontributory.

Eye examination: V.R.E. 20/20; V.L.E. 20/20.

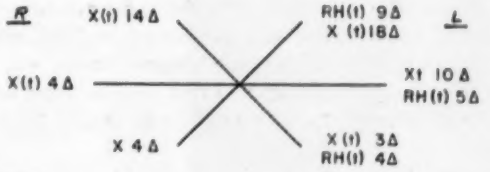
Refraction (cycloplegic): R. $+0.50-0.25\times165^{\circ}$

L. $+0.50-0.75\times 15$

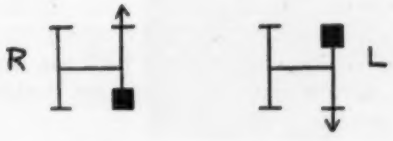
External examination: Negative save for right shoulder drop and neck to left.

Muscle balance: Distance (uncorrected): 2Δ E; near (uncorrected): 1Δ E RH^{t} 2Δ.

Cardinal positions:



Screen and cover:



Bielschowsky test: Positive to right shoulder.

Leg measurements: Equal right and left.

X-rays: Slight dorsal scoliosis to right, thoracolumbar left. No skeletal abnormality (Fig. 8).

Fig. 8 (Case 4).—Spine.

Ophthalmoscopic examination: Negative, O.U.

Impression.—Right superior oblique weakness. Right hypertropia when looking to the left.

Program.—Glasses with prisms were attempted unsuccessfully. Orthoptics were not feasible owing to occupation. A myomectomy of the right inferior oblique was performed, and immediately postoperatively the vertical component in the primary position was zero. Six months after operation vision was orthopic, for distance and near.

Case 5.—A 9-year-old white girl with the right eye turned up and in from birth. Recessions of both interni were performed in 1948, with a postoperative exophoria and right hyperphoria, but third-degree fusion was maintained in the head-tilted position. The previous report listed an overaction of the right inferior oblique, but no evaluation of the component was made. Past history was noncontributory.

Eye examination: V.R.E. 20/40; V.L.E. 20/30.

Refraction (cycloplegic): R. $+1.50+0.75\times105=20/20$

L. $+1.00+0.50\times\ 90=20/20$

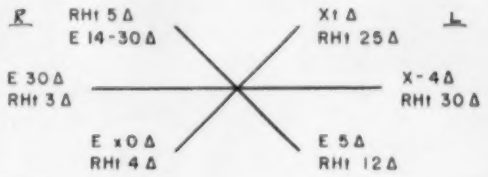
External examination: Negative except a head and neck tilt to the left with a shift of the lower thoracic spine to the left and lumbar to the right. There was a definite right shoulder drop.

Muscle balance:

Distance (uncorrected)	E¹ 2Δ	(corrected) E 3Δ RH 3Δ
Near (uncorrected)	E¹ 28Δ	(corrected) E 2Δ RH 4Δ
	RH¹ 16Δ	(vertical prisms)

N.P.C. 110 mm.

Cardinal positions (left eye fixing):



Screen and cover:

With the right eye fixing there is an underaction LSR.

Bielschowsky test: positive to right shoulder with downward shift of left eye to left shoulder.

Leg measurements: Right leg, 26½ in.; left leg, 26½ in. (anterior superior spine to lateral malleolus).

Spinal x-rays: lower thoracic scoliosis to left. No bony abnormality (upright) (Fig. 9).

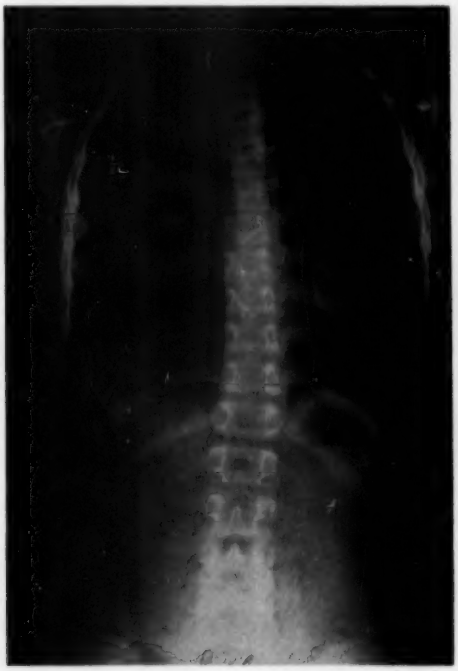


Fig. 9 (Case 5).—Spine.

Impression.—Esotropia, intermittent, accommodative; right hypertropia due to weakness of right superior oblique.

Program.—A myomectomy of the right inferior oblique was performed on June 21, 1955. Results on March 14, 1956, were as follows:

Distance (uncorrected)	E 4Δ	(corrected) E 1Δ
	RH 1/2Δ	(corrected) X −2Δ
Near (uncorrected)	Ortho.	RH 1/2Δ

CASE 6.—An 11-year-old white boy had been told that he must have had a broken collarbone at birth, because an abnormal head position was noted shortly thereafter. The mother noticed that the left eye was lower than the right from the beginning. The right inferior oblique had been operated upon. Past history was noncontributory.

Eye examinations: V.R.E. (uncorrected) 20/20−2
V.L.E. (uncorrected) 20/30+3

Refraction (cycloplegic): R.+1.00+0.25×90=20/20
L.+0.50+0.25×90=20/20

External examination: Essentially negative except for marked head tilt to left shoulder with large right hypertropia in all fields of gaze. Face tilt left, chin depression, right shoulder drop.

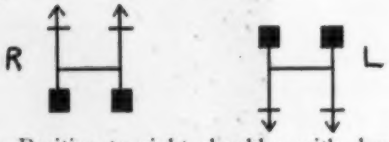
Ophthalmoscopic examination: Negative, O.U.

Muscle balance: N.P.C. remote. Alternates but prefers R.E. (distance and near).

Distance (uncorrected)	E^t 5Δ	RH^t 12Δ-16Δ
Near (uncorrected)	E^t 2Δ	RH^t 30Δ-35Δ

Cardinal positions:

Screen and cover:



Bielschowsky test: Positive to right shoulder with downshoot of left eye to right shoulder.

Leg measurements (anterior superior spine to lateral malleolus): Equal right and left.

X-rays: No bony abnormality. Scoliosis involving lower thoracic and lumbar areas to left (Figs. 10 and 11).

Impression.—Alternating esotropia with right hypertropia. Right superior oblique palsy with inhibitional palsy of the left superior rectus and weakness of right inferior rectus.

Program.—A myomectomy of the right inferior oblique was performed on Aug. 16, 1955, and immediately postoperatively the hyperphoria was as follows: Distance: RH 6-8 D.; Near: RH 7-16 D. The head tilt remained, and the RH definitely increased with the head in an erect position. Five months postoperatively the figures were essentially the same.

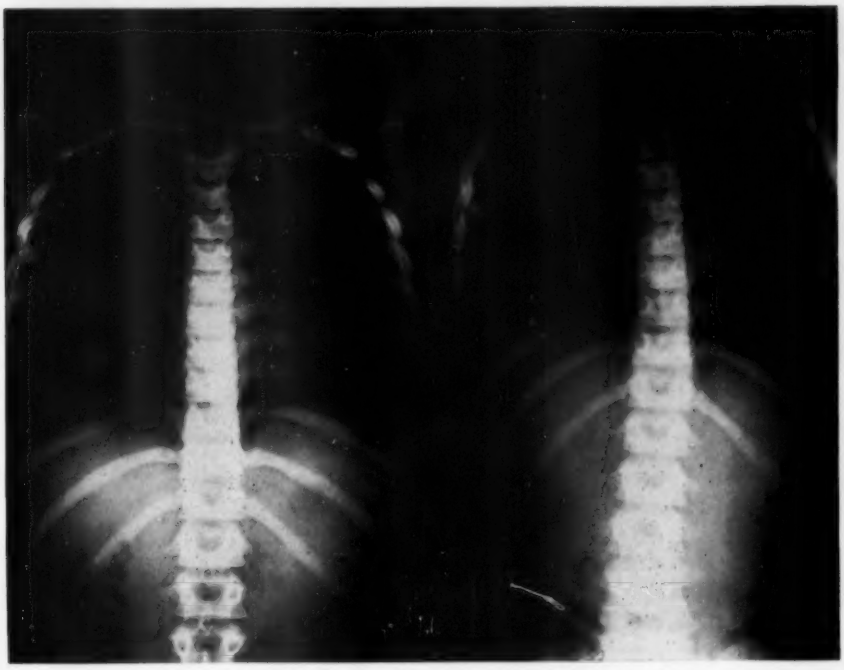


Fig. 10 (Case 6).—Upper spine. Left, lying; right, standing.

Fig. 11 (Case 6).—Lower spine. Left, lying; right, standing.

CASE 7.—A 12-year-old white girl whose right eye had turned in from birth. A bilateral medial rectus recession was performed, with a postoperative exotropia. A secondary resection and advancement of the right internus was performed, with a left hyperphoria and exotropia noted postoperatively. Past history was noncontributory.

Eye examination: V.R.E. 20/30−2; V.L.E. 20/30−2.

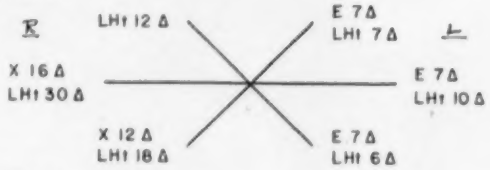
Refraction (cycloplegic): R.+1.50+0.75×120=20/20
L.+2.00+0.75× 75=20/20

External examination: Negative save for medial rectus scars, a right shoulder drop, and head tilt to right shoulder.

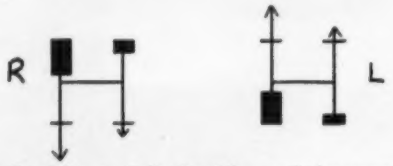
Muscle Balance:

Distance (uncorrected)	E^t	12Δ	(corrected)	X 4Δ
	LH^t	16Δ		LH^t 10Δ
Near (uncorrected)	E^t	14Δ	(corrected)	E^t 5Δ
	LH^t	12Δ		LH^t 10Δ

Cardinal positions:



Screen and cover:



Bielschowsky test: Positive to left shoulder and downward movement of right eye to the left shoulder.

Ophthalmoscopic examination: Negative, O.U.

Leg measurements: Equal right and left.

Spine x-rays (Fig. 12): No bony abnormality, but S-shaped scoliosis of thoracic spine to right (apex T4), lumbar curve left (apex T12-L1).

Impression.—Accommodative esotropia with left hypertropia caused by weakness of left superior oblique and contralateral inhibitional palsy of right superior rectus. Surgical weakness of left medial rectus.

Program.—On July 1, 1955, a myomectomy of the left inferior oblique was performed. On Oct. 27, 1955, muscle balance was as follows:

Distance: X 2Δ
LH^t 8Δ
Near: X 2Δ
LH^t 6Δ

This was corrected by prisms.

CASE 8.—A 3-year-old boy with eyes turning in for about one year. Past history was noncontributory.

Eye examination: V.R.E. 6/12; V.L.E. 6/9. ("E")

Refraction (cycloplegic): R.+2.00+0.25×90
L.+1.00+0.50×90

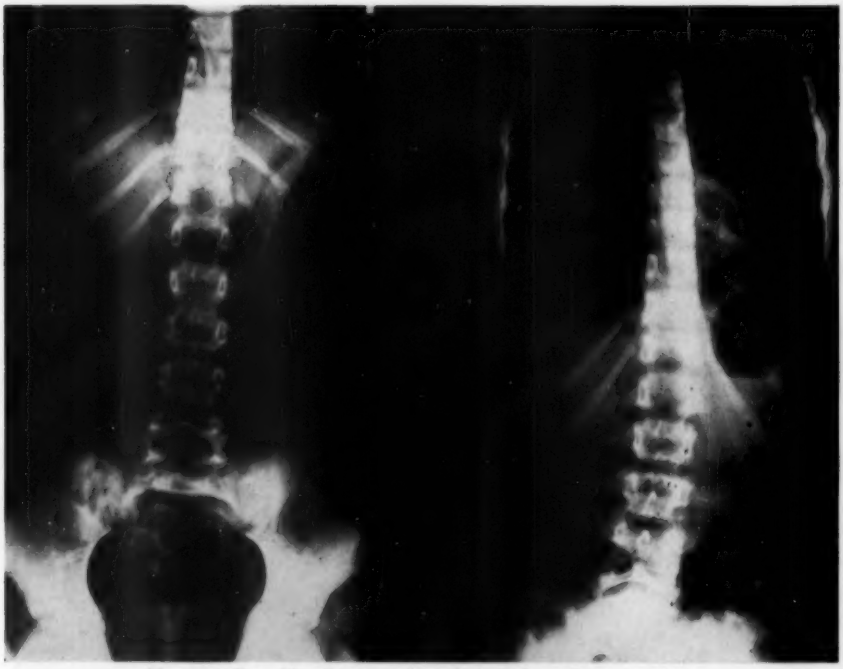


Fig. 12 (Case 7).—Lower spine. Left, lying; right, standing.

External examination: Negative except for an alternating ET.

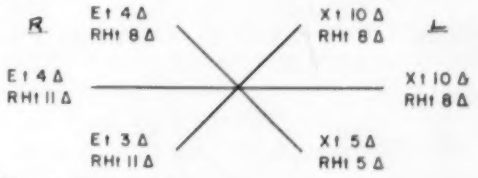
Muscle balance:

Distance (uncorrected)	E^t 38Δ	(corrected)	E 18Δ
			RH^t 2Δ
Near (uncorrected)	E^t 36Δ	(corrected)	E^t 25Δ
	RH (?)		RH (?) Δ

A right medial rectus recession was performed on Nov. 12, 1952, seven months postoperatively.

Distance (uncorrected)	(corrected)
E^t 6Δ	E^t 8Δ
RH^t 5Δ	RH^t 5Δ
Near (uncorrected)	(corrected)
(and vertical clip-ons)	
X^t 10Δ	X^t 2Δ
RH 1Δ	RH 1Δ

Cardinal positions:



RH^t equal for distance or near.

Screen and cover (left eye fixing):

There was a left shoulder drop and head tilt to the left with chin depression and slight face turn to right.

Bielschowsky test: Slight positive to right shoulder.

Leg measurements (anterior superior spine to lateral malleolus): Equal right and left, 24½ in.

X-rays: No bony abnormality except for a dorsolumbar deviation of the spine to the right (Fig. 13).

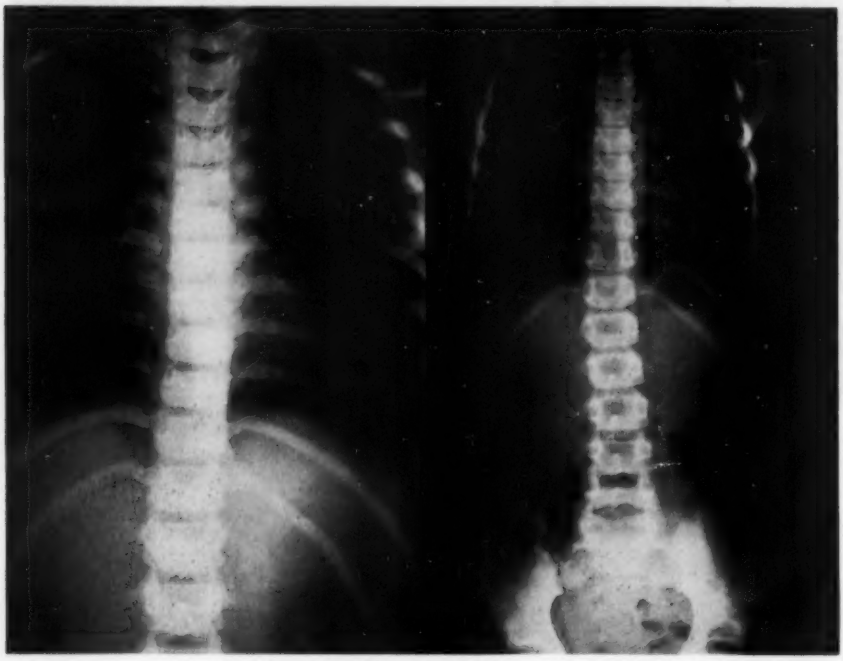


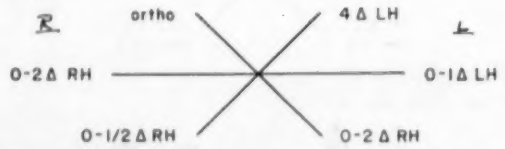
Fig. 13 (Case 8).—Spine. Left, lying; right, standing.

Impression.—Esotropia, partially accommodative, alternating, with right hypertropia due to right superior oblique weakness and right inferior rectus weakness.

Program.—On Jan. 7, 1955, a recession of the left inferior oblique was performed. On Nov. 16, 1955, V.R.E. 20/20; V.L.E. 20/20. Muscle balance was as follows:

Distance (uncorrected)	E^t 1-4Δ RH 1-2Δ	(corrected) X^t 4Δ RH 2Δ
Near (uncorrected)	E^t 3Δ LH 1-2Δ	(corrected) X 3-7Δ

Cardinal positions:



Case 9.—A 29-year-old white man was first seen at the age of 16, at which time he was found to have a right superior rectus and right levator palsy ap-

parently existing from birth. A right superior rectus tuck and right medial rectus recession was performed. Five months later a Traintor procedure for ptosis was performed. The ptosis and superior rectus weakness persisted, with diplopia in all fields of gaze. V.R.E. 15/30; V.L.E. 15/15. A resection of the right superior rectus was performed, followed by a recession of the right lateral rectus and recession of the inferior oblique, right eye. The left hypertropia persisted in all fields of gaze, but some control could be obtained if the head was tilted to the left and back with a face tilt left. Even in this position there was a definite protective ptosis. The patient had a severe postural defect and a great deal of trouble driving. Past history was noncontributory.

Eye examinations: V.R.E. 20/100 (uncorrected)
V.L.E. 20/100 (uncorrected)

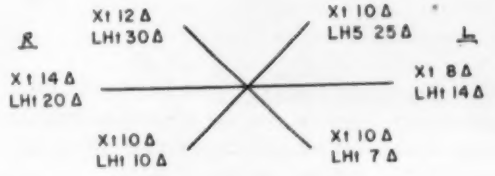
Refraction (cycloplegic): R.$-5.00-3.25\times 15=20/50+1$
L.$-4.00-1.25\times 100=20/20$

External examination: Definite protective ptosis, right eye, which is partially levator weakness. There is a marked head tilt to the left with chin elevated and face tilt left. The remainder of external examination is negative.

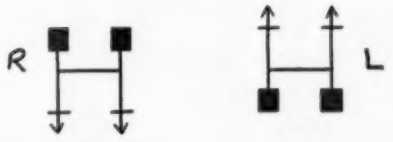
Muscle balance:

Distance (uncorrected)	X^t 12Δ		(corrected)	X^t 10Δ
	LH^t 22Δ			LH^t 20Δ
Near (uncorrected)	X^t 14Δ		(corrected)	X^t 10Δ
	LH^t 12Δ			LH^t 10Δ

Cardinal positions:



Screen and cover:



Bielschowsky (head-tilting test): To right shoulder very slight upward movement, right eye. Marked downward movement, left eye. To left shoulder essentially no vertical movement (reg. test).

Leg measurements: Equal right and left.

Spine x-rays: These revealed no skeletal abnormality but a definite dorsal scoliosis to the right with a thoracolumbar curve, apex to the left (Fig. 14).

Impression. (1) Right superior rectus and right levator paresis, congenital; (2) right inferior oblique paresis, surgical; (3) underaction of left superior oblique and left inferior rectus with overaction of right inferior rectus and right superior oblique, left superior rectus and left inferior oblique.

Fig. 14 (Case 9).—Lower spine. Standing.

Case 10.—A 5-year-old white girl was seen for a general examination. A head tilt with irregular cranial shape had existed from birth. Labor lasted 36 to 40 hours. Past history was noncontributory.

Eye examination: V.R.E. 20/20; V.L.E. 20/20.

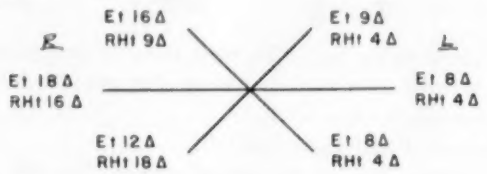
"E" Refraction (cycloplegic): R. +0.50+0.25×90; L. +0.50+0.25×90.

External examination: Negative save for obvious prominence of right frontal area, chin depression with head tilt to left and face tilt right.

Muscle balance: N.P.C. remote; prefers O.S.

Distance (uncorrected)	E^t	12Δ
	RH^t	5Δ-LH
Near (uncorrected)	E^t	18Δ
	RH^t	9Δ-LH

Cardinal positions:



Screen and cover:

Bielschowsky test: Negative.

Leg measurements: Equal right and left, 22½ in.

X-rays: Skull shows plagiocephaly. Spine shows an S-shaped curve to right in lower thoracic area and curves to left in thoracolumbar area. No skeletal abnormality (Fig. 15).

Fig. 15 (Case 10).—Spine.

Ophthalmoscopic examination: Negative, O.U.

Impression.—Esotropia, alternating, but left eye preferred, with right hypertropia caused by right inferior rectus weakness.

Program.—On Aug. 19, 1955, a right medial rectus recession and right superior rectus recession were performed. On Jan. 24, 1956, V.R.E. 20/20; V.L.E. 20/20.

Muscle balance:

Distance	E^1	2Δ
	LH	3Δ
Near	E^1	7Δ
	RH	3Δ-DH

Case 11.—A 9-year-old white boy has had a weak muscle of the right eye since birth. No eye complaints except that the patient is a poor student. Past history was noncontributory.

Eye examination: V.R.E. (uncorrected) 20/20−2; V.L.E. (uncorrected) 20/20−1.

Refraction (cycloplegic): R.−0.25; L.−0.25.

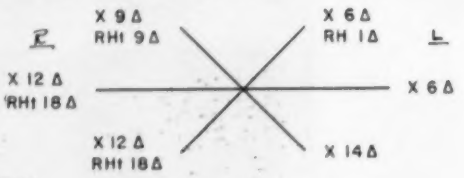
External examination: Negative save for head tilt to right, chin depression and face tilt to right.

Muscle balance:

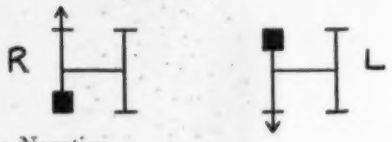
Distance (uncorrected) X 1Δ RH 3Δ

Near (uncorrected) X^{t} 12Δ RH 3Δ

Cardinal positions (prefers right eye):



Screen and cover:



Bielschowsky test: Negative.

Leg measurements (anterior superior spine to lateral malleolus): Equal right and left, 30¼ in.

X-rays: Scoliosis to left, upper thoracic area. Scoliosis to right, lower thoracic area. The curve increases in the standing position. No bony abnormality (Fig. 16).

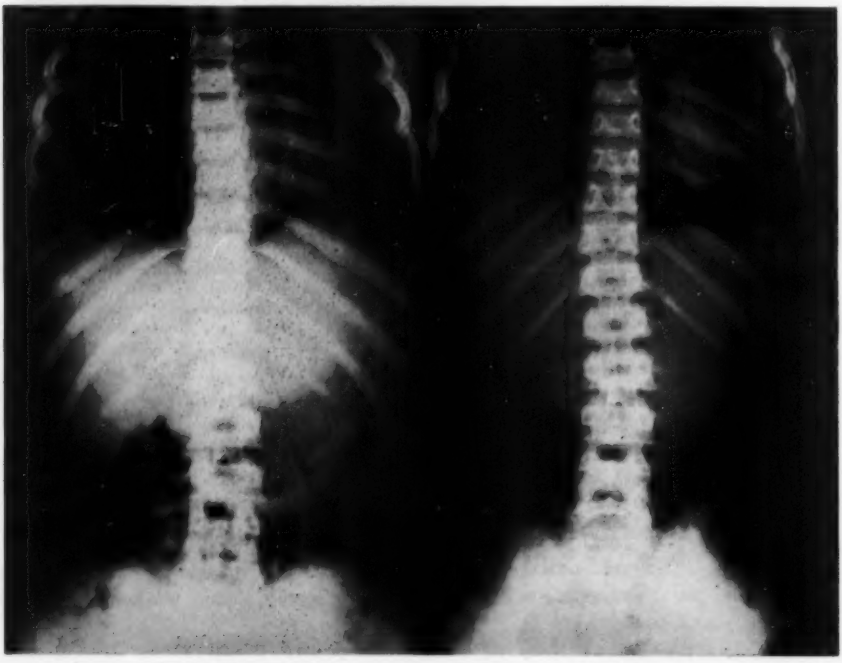


Fig. 16 (Case 11).—Lower spine. Left, lying; right, standing.

Ophthalmoscopic examination: Negative, O.U.

Impression.—Right inferior rectus weakness, intermittent exotropia for near.

Program.—A recession of the right superior rectus was performed Sept. 9,

1955. Six months postoperatively muscle balance was as follows:

Distance (uncorrected)	X	1Δ
	LH	2Δ
Near (uncorrected)	X	6Δ
	LH	2Δ

with good fusional amplitude.

CASE 12.—A 7-year-old white boy with no known muscle imbalance. Past history was noncontributory.

Eye examination: V.R.E. 20/20; V.L.E. 20/20.

"E" Refraction (cycloplegic): R.+1.00+0.37×180; L.+1.00+0.25×180.

External examination: Negative, O.U., except for face turn to right shoulder and head tilt to left shoulder.

Bielschowsky test: Negative.

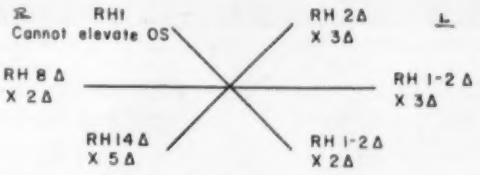
Muscle balance: Fuses in all positions from tilted position of head except up and right, where patient is able to suppress. N.P.C., to nose. Fusion range:

Distance	Near
ABD 4	ABD 10
ADD 25	ADD 30

Distance (uncorrected) RH 5Δ

Near (uncorrected) RH 8Δ×1Δ

Cardinal positions:



Ophthalmoscopic examination: Negative, O.U.

X-rays: Normal bone structure. Dorsal scoliosis to the right in standing position (Fig. 17).

Leg measurements (anterior superior spine to lateral malleolus): Right leg, 25 in.; left leg, 25 in.

Impression.—Left inferior oblique palsy.

Program.—Recession of right superior rectus. Postoperatively vision is binocular in all positions of gaze, head erect, except up and right.

Comment

There are several points which apply to the general series:

1. The abnormality in every case was noted at birth or shortly thereafter.

2. Involvement of any one or of several vertically acting muscles may induce head tilting. This in turn will cause a compensatory shift of the spine to neutralize the cervical angulation. The S-shaped curve of the spine apparently is an attempt on the part of the person to maintain the erect posture essential for coordination; e. g., walking, etc. If the neck bend is to the right the upper thoracic bend will be left; lower thoracic, right, and lumbar, left. Usually the most marked curve is in the thoracolumbar and cervical areas.

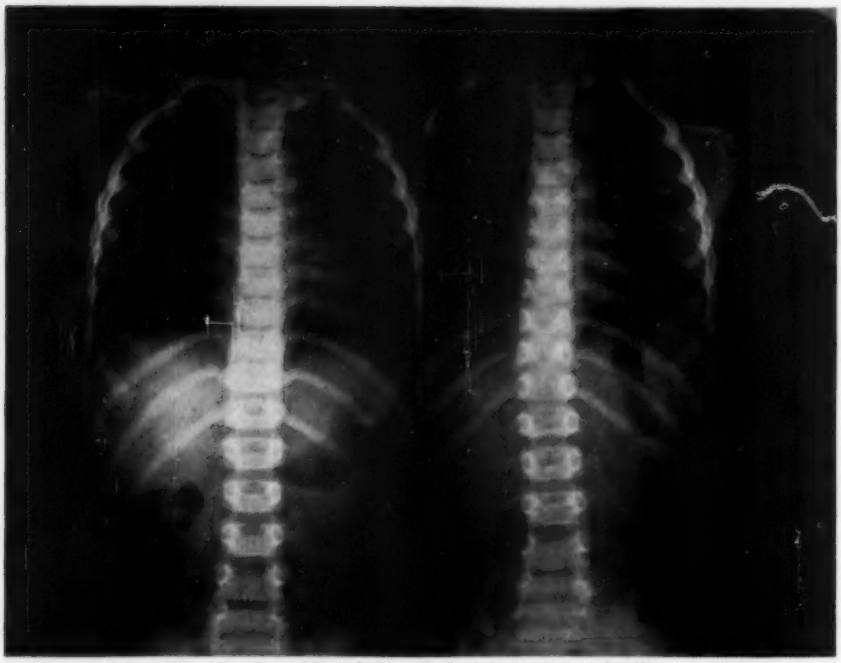


Fig. 17 (Case 12).—Spine. Left, lying; right, standing.

3. In every case studied to date the leg measurement (from the anterior superior spine to the lateral malleolus) was equal right and left.

4. No abnormality of the vertebral column or pelvis was found in any case. Therefore the scoliosis is muscular in origin.

5. The cases may be divided into four groups:

Group I. Superior oblique-superior rectus syndrome. These cases are so named because the superior oblique appears to be the primary muscle at fault. Underaction of the superior rectus is noted with screen and cover, the head fixed in an upright position. This is noticeable even though the paretic eye is not always the fixing eye.

(*a*) Those who have maintained fusion in the primary position. (Cases 1-5) There is a hyperphoria greater for near. Usually there is a large hypertropia to one side, both up and down, and little if any to the opposite side. Head tilt is to the side opposite the paretic muscle with chin depressed. The Bielschowsky head-tilting test is positive to the paretic side. A definite underaction of the superior rectus is noted in its cardinal position because of the relative overaction of the inferior rectus on the same side and the overaction of the inferior oblique on the paretic side.

(*b*) The cases which were not able to maintain fusion in any position of gaze. Each of these cases had a hypertropia of the same type in all fields of gaze. In every one of these cases the vision was equal and there was a horizontal deviation as well. In nearly every case the horizontal error was an alternating esotropia. The horizontal error would appear to be secondary to the vertical error in most cases, even though the ophthalmologist

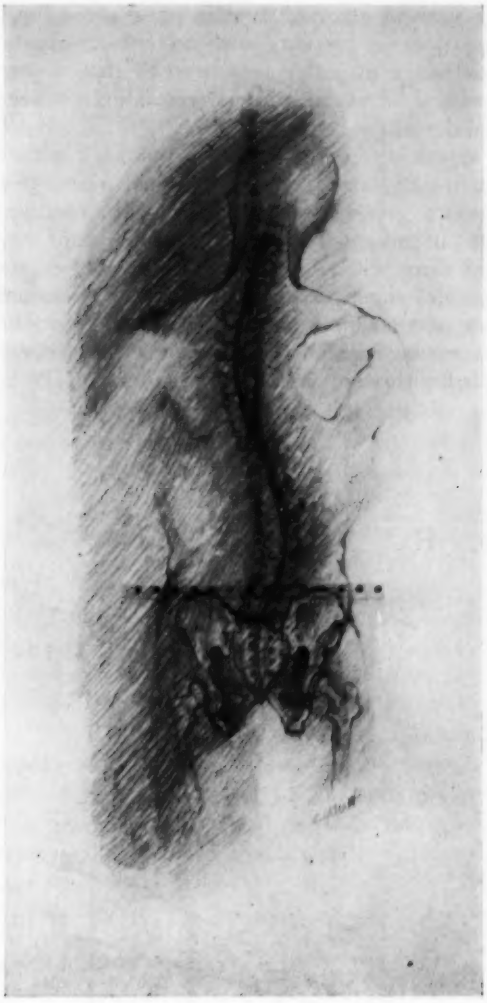


Fig. 18.—Artist's interpretation.

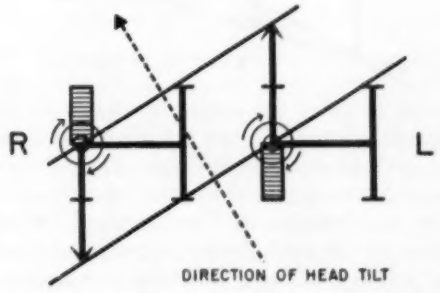


Diagram 1.—Fusion attained; parallelism attained.

"uncovered" the vertical error after attempting correction of the horizontal error. The vertical error presents such an uncomfortable problem for the infant insofar as image disparity is concerned that a secondary horizontal deviation is necessary for visual comfort (rotational disparity may be reduced by the horizontal deviation).

These cases appear severer in degree as compared with (*a*). Possibly the superior oblique weakness is more pronounced or foveal demand is insufficient. This entails a greater rotatory defect with resultant excessive excyclotorsion. Head tilt and superior rectus underaction of the opposite eye will be noticeable, but there will also be compensatory development of a superior oblique (normal side)-superior rectus (paretic side) overaction in an attempt to attain rotatory parallelism of the eyes. For example, left superior oblique-right superior rectus weakness with left inferior oblique, right inferior rectus overaction coupled with right inferior oblique-left inferior rectus underaction and right superior oblique, left superior rectus overaction.

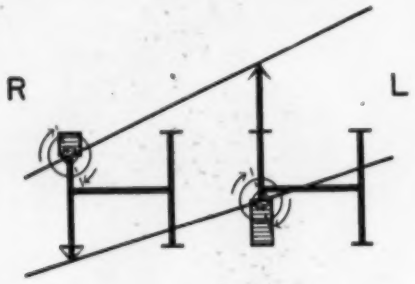


Diagram 2.—Fusion not attained; parallelism not attained.

A possible course of events is as follows: First, in Diagram 2, there is weakness of the superior oblique. In the primary position this will cause an excessive excyclorotation of the paretic eye from the overaction of the homo-

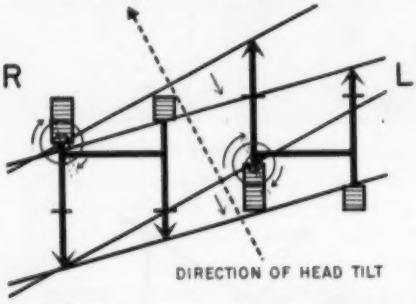


Diagram 3.—Fusion not attained; parallelism not attained.

lateral inferior oblique. A tendency to tilt the head to the opposite shoulder is not enough for cyclorotatory parallelism. The relative overaction of the contralateral inferior rectus and underaction of the superior rectus will not effect the necessary incyclorotation. Therefore, in Diagram 3, incyclorotation is effected by action of the contralateral superior oblique with inhibition of the corresponding inferior oblique. The superior rectus of the paretic eye will then be relatively overacting, while the corresponding inferior rectus

will be inhibited. This will bend itself to relative cyclorotatory parallelism, which is finally attained in Diagram 4. These cases will have a nearly con-

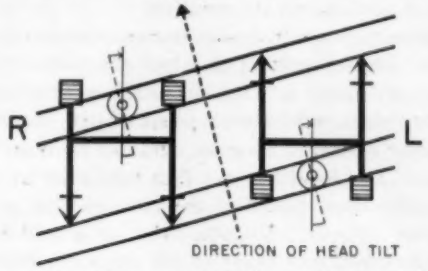


Diagram 4.—Fusion not attained; parallelism attained.

stant hypertropia in all fields of gaze, and the head tilt may seem reduced. However, the compensatory demands upon the spine remain in order to allow as little vertical disparity as possible.

The greater the need for ocular cyclorotation the greater the necessary head tilt and subsequent spinal adjustment (Cases 6-8).

Group II. Superior rectus-superior oblique syndrome (superior rectus primary underaction, superior oblique underaction of ipsilateral eye). These cases are similar to those in Group I except for the hypertropia greater for distance than near, the negative Bielschowsky test, and the association with other oculomotor stigmata. These cases may have a horizontal error also, usually exotropia due to the loss of adducting power (Case 9).

Group III. Inferior rectus-inferior oblique syndrome (primary inferior rectus underaction with contralateral inferior oblique underaction).—The success or failure of fusion is again evident in these cases. The head tilt is to the same side as the oblique weakness, and the Bielschowsky test is negative (Cases 10 and 11).

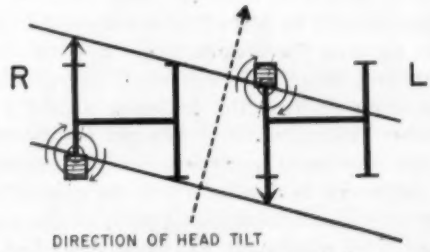


Diagram 5.—Fusion not attained; parallelism attained.

Group IV. Inferior oblique-inferior rectus. The opposite of Group III. Again fusion may or may not be present in the primary position (Case 12).

6. The greater majority of cases are due to superior oblique weakness rather than superior rectus weakness; however, the two muscles are involved together in many cases, presenting a "superior oblique-superior rectus syndrome." This apparently evolves from a primary weakness of the superior oblique, with paretic eye fixing and inhibitional palsy of the contralateral antagonist. It is much more logical to expect the superior oblique to be affected, for several reasons: (*a*) The fourth nerve has a longer intracranial course than the third and is therefore more easily damaged. (*b*) The

muscle itself is more vulnerable in the orbit. (*c*) If the superior rectus were involved primarily, one would expect to see involvement of the levator or some other segment of oculomotor innervation.

7. Ophthalmologists may confuse superior rectus involvement for superior oblique involvement. This may happen when the patient alternates or fixes with the paretic eye, or it may be seen when the patient can fuse in the primary position. In any case, inhibitional palsy of the contralateral antagonist —superior rectus—may occur. This may actually be more pronounced than the oblique weakness. The head tilt and face turn may be the same (though different in degree) with involvement of the two muscles, e. g., right superior rectus or left superior oblique. Usually, the chin will be depressed with superior oblique weakness. Since many of the cases get into adulthood before discovery or else are uncovered after correction of horizontal errors, there has been plenty of time for the sequelae of an extraocular muscle palsy to assume relative comitance. The measurements for distance and near and in the cardinal positions may indicate a large hypertropia in the area of both superior rectus and superior oblique, and with this there will be modification of the adopted head posture (Chavasse [6]).

8. The forced head-tilting test of Bielschowsky oftentimes is overlooked or not properly performed. For it to be done properly, the patient must be comfortably seated in a chair. With the patient fixing on a target (approximately 20 ft.) the head is forcibly tilted to one shoulder and then the other, and vertical movement of one eye or the other is noted. The body must not be allowed to bend and so the head-shoulder relationship is effectively changed 90 degrees. Fixation on the distant target must be maintained. In many cases the test as performed in this manner is inconclusive. This occurs because the muscular development on the tilted side of the neck restricts movement to the opposite side. Since adequate head tilt must take place in order for vertical movement to be detected, a possible false negative may result. If the patient is unable to bend the head properly from side to side, then the patient's head should be placed on the shoulder, and, with the head so fixed, the eyes are fixed on the distant target and the observer alternately covers the eyes. This will bring out even small degrees of excess elevation from one side to the other (in case the deviation is only a phoria in the primary position). Another feature which is brought out by performing the test in this manner is the downward movement of the opposite eye when the head is tilted to the same side as that on which the upward movement occurs. This is seen in those cases with inhibitional palsy of the contralateral antagonist-superior rectus. The movement has been described by Chavasse in isolated superior rectus palsy (Duke-Elder [7]).

9. Many of the cases have an esotropia. Since most of the cases presented are due to superior oblique paresis, the reason would appear to be the excessive adduction with loss of superior oblique abducting power.

10. The ocular abnormality in every case was first noted shortly after birth. Since the macular areas develop at about 5 to 6 months of age and bifixation shortly thereafter, the desire for fusion appears before the child walks and possibly before it can sit upright. Therefore, the desire for fusion causes adjustment of the entire body above the pelvis. This adjustment is made by the muscles of the back and neck as an attempt to maintain the vertical body position which is required for normal locomotion and balance.

Even though fusion is not maintained and there is no bony abnormality, the scoliosis does not disappear. This may be due to the continued demand for cyclorotatory parallelism.

11. The x-rays were taken standing and lying. When the patient is erect and fixing some target with his eyes, the scoliosis is more pronounced. The lying position allows for neutralization of the upright spinal contour.

12. The treatment of these cases is not a part of this paper. Suffice it to say that in those cases with the superior oblique-superior rectus syndrome the treatment has been the same, surgical myomectomy of the inferior oblique on the involved side, e.g., in a case of left superior oblique paresis, left inferior oblique myomectomy as a primary procedure. This usually reduces the vertical component in half. However, even though the posture is improved, the scoliosis persists. Treatment must be directed primarily at the cyclorotatory defect.

13. There are several types of vertical muscle imbalance in which scoliosis usually is not noted. These fall into the bilateral hypertropia or double hypertropia groups, and there are two basic types:

I. Bilateral superior oblique-superior rectus weakness. In this case the

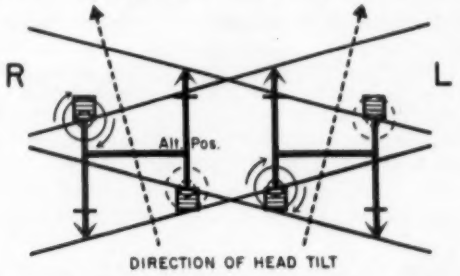


Diagram 6.—Fusion not attained; parallelism attained.

patient will freely alternate, parallelism will be attained, and there will not be a constant head tilt and, therefore, no scoliosis.

II. Bilateral inferior oblique-inferior rectus weakness. The patient also also has an alternating hypertropia. There is no constant head tilt. Parallelism (rotatory) is attained on alternate fixation. Scoliosis is not noted.

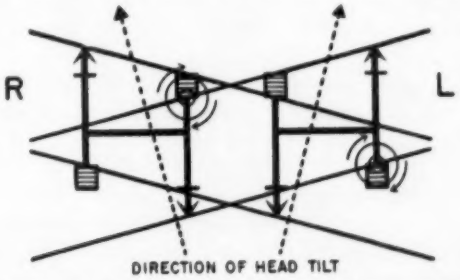


Diagram 7.—Fusion not attained; parallelism attained.

Summary and Conclusions

Scoliosis of the vertebral column occurs with weakness of any one or pair of the vertically acting muscles causing excessive cyclorotation of the eye.

Neutralization of this defect is necessary for ocular rotational parallelism. This results in "ocular torticollis" and compensatory scoliosis.

Superior oblique-superior rectus involvement is commonest.

There is no bony abnormality, and the spinal shift apparently compensates for the head tilt in order for the person to maintain an erect posture.

The cases may be divided into two groups: those who maintain fusion and those who do not. The maintenance of fusion is not necessary in order for the scoliosis to persist.

The scoliosis apparently develops shortly after birth in response to a desire for ocular bifixation.

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Announcement of Awards

Several awards were made by the Executive Committee of the Section on Ophthalmology at the 105th Annual Meeting of the American Medical Association, Chicago.

1. The Prize in Ophthalmology. The following remarks were made by Dr. Trygve Gundersen in presentation:

"It is my signal honor as chairman of your executive committee to present this medal, 'The Prize in Ophthalmology,' to our beloved friend and leader Derrick T. Vail. Nothing could possibly give me greater pleasure. It would require a major opus to sing of the accomplishments of this illustrious man. To point out all his accomplishments would indeed take much research and writing, perhaps even more time than that allowed by our constitution and bylaws. Offhand when one thinks of his accomplishments a flood of important contributions and a flood of recollections of jobs well done come to mind. His thousands of patients would naturally acclaim him as their doctor—those whose sight he has restored, those whose vision he has preserved, those whose eyes he has straightened, and even those whose glasses he has kept in perfect adjustment through the years. Truly as a practicing physician opthalmologist he has no peer.

"His efforts as a teacher have been equally illustrious. Dr. Vail has developed not only one but two large ophthalmology departments in important schools of medicine. They are now great teaching centers. One might add to this his outstanding efforts in postgraduate teaching and his tireless efforts with the American Board, of which he has been a member for so many years.

"Of scientific contributions there have been so many that to list them here would be impossible. He has truly graced and embellished every branch of our specialty. As a patriot Derrick likewise has had no equal. Like the Father of his Country he has indeed been 'First in War, first in Peace, and first in the hearts of his countrymen.'

"Each of these facets of his life work could be the subject of a dissertation. I need only mention Derrick T. Vail and the *American Journal of Ophthalmology* looms before us. A journal which was once called 'that yellow sheet' is now required monthly reading for 16,000 ophthalmologists in these United States alone.

"In order to give you an idea of what a full life this great man leads, let me list only a few of his present extracurricular activities: Vice-President, American College of Surgeons; Member, National Institute of Health and Blindness; Chairman, Special Medical Advisory Group to V.A.; Member, Committee on Ophthalmology, National Research Council; Honorary Fellow, Royal College of Surgeons.

"I believe we all like to think of Derrick as our leader, our spokesman, our torchbearer. Indeed, if any phrase fits him I believe it is, our champion. Therefore, to you, Derrick T. Vail, I have the great honor to present this beautiful medal, with the love and affection of us all."

2. The $250.00 prize for the best exhibit was awarded to Bertha A. Klien, "Survey of the Pathogenesis of Retinal Vein Occlusions."

3. The $250.00 prize was awarded to T. E. Sanders for his paper, "Fungus Keratitis," judged on the basis of presentation and originality.

The following officers were elected: Chairman, Algernon B. Reese; Vice-Chairman, Hedwig S. Kuhn; Secretary, Harold G. Scheie; Representative to Scientific Exhibit, Frank W. Newell; Delegate to House of Delegates, Ralph O. Rychener; Alternate Delegate, Harvey E. Thorpe.

Hypophysectomy for Diabetic Retinopathy

A Preliminary Report

ROBERT A. SCHIMEK, M.D.
Detroit

Diabetic retinopathy has become one of the most frequent causes of progressive, incurable blindness. Because of the urgency of this subject, this preliminary report is submitted of five cases treated in a new and radical fashion. This radical treatment consists of hypophysectomy, or surgical removal of the pituitary. The postoperative progress of the retinopathy in these cases suggests a possible beneficial effect, especially with regard to retinal and vitreous hemorrhages. However, the cases are too few, with retinopathy too advanced or follow-up too short, to permit anything approaching adequate evaluation.

Chabanier [1] was the first to report hypophysectomy on a diabetic patient. Hypophysectomy for diabetic retinopathy and nephropathy has been reported by Luft * (20 cases) and Kinsel [4] (4 cases). After hypophysectomy in Luft's series,† vision usually remained about the same or improved slightly. In 22 eyes of 11 patients followed from 3 to 24 months, vision improved in 8 eyes, remained the same in 10 eyes, and became worse in 4 eyes by objective measurement. The retinopathy usually remained stationary as judged by its ophthalmoscopic appearance, but occasional regression as well as progression was reported.

Hypophysectomy is not only lacking in adequate clinical evaluation of its effect on retinopathy but also carries some risk and dooms the patient to a lifetime of glandular replacement therapy. It need be emphasized that, at present, hypophysectomy is not being recommended for patients with diabetic retinopathy except as a radical, experimental procedure of unproved value. It is justifiable only if the patient understands the dangers involved and the probability of his not being helped.

Possible Modes of Action of Hypophysectomy on Diabetic Retinopathy

There is much evidence to suggest that hypophysectomy might influence the course of diabetic retinopathy. For example, hypophysectomy will reduce adrenal function. This might be indicated, since high adrenal function accompanies and perhaps may help cause diabetic retinopathy.‡ Also, hypophysectomy may be indicated because abnormal function of the pituitary itself can cause diabetes and may be a direct factor in the causation of diabetic retinopathy.

Evidence for Adrenal Hyperfunction in K.W.-D.R. Group

First, let us review the evidence for increased adrenal function in diabetics with retinopathy. The Kimmelsteil-Wilson (K. W.) vascular lesion in the kid-

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Presented before the 15th Annual Meeting of the Wilmer Residents Association, Baltimore, April 19, 1956.

* References 2 and 3.

† References 2 and 3.

‡ References 5 and 6.

ney [7] has a very high incidence in diabetics with retinopathy (D. R.) and is rare in diabetics without retinopathy.§ Experimentally, cortisone produces lesions of the Kimmelsteil-Wilson type in rabbits.‖ Kimmelsteil-Wilson lesions have also been produced by desoxycorticosterone acetate administration in alloxan-diabetic rabbits.[14] Nondiabetic patients who had been under prolonged corticotropin therapy have shown lesions of the Kimmelsteil-Wilson type at autopsy.¶ Other autopsy studies showed that the Kimmelsteil-Wilson group of diabetics have increased adrenal weight or adrenal hypertrophy,[5] increase in vacuolization of the adrenal zona fasciculata,[15] and an increased incidence of adrenal cortical adenomas.# These all suggest increased adrenal cortical function in diabetics with Kimmelsteil-Wilson lesions. Clinically, patients with diabetic retinopathy and Kimmelsteil-Wilson lesions show increased 11-oxysteroid excretion in the urine.*

Other Evidence for Adrenal Hyperfunction in Diabetics with Retinopathy

Another suggestive finding is that the α_2-globulin is significantly elevated in diabetics with retinopathy † as compared with that of normals and with that of diabetics without retinopathy. The α_2-globulin fraction is rich in hexose amine, which other workers have found to be increased in diabetics with retinopathy.[15]

When cortisone is given to rabbits, the α_2-globulin fraction of rabbit serum increases.‡

In recent years, saccular microaneurysms of the retinal capillaries have commonly been stated to be a characteristic vascular lesion of diabetic retinopathy.§ Retinal microaneurysms have been found in some cases of adrenal hyperplasia, and they have been described ophthalmoscopically in some patients on long-term corticotropin therapy.‖

Diabetic retinopathy has been reported aggravated by pregnancy,[24] improved after bilateral adrenalectomy,[25] and improved after spontaneous pituitary atrophy [26] (which in turn causes adrenal atrophy). The high 11-oxysteroid urinary excretion in patients with diabetic retinopathy [18] is suggestive of high adrenal function. Many diabetics without retinopathy have a poor adrenal response to corticotropin,¶ a low cyanocobalamin (vitamin B_{12}) excretion rate,[27] and pantothenic acid deficiency.# It has been suggested these findings may indicate adrenal hypofunction in diabetics without retinopathy.

§ References 8-11.

‖ References 12-15.

References 15 and 16.

¶ Rich, A. R.: Data presented at Johns Hopkins Hospital Clinical-Pathological Conference, February, 1952.

* References 17 and 18.

† Lerman, S., and Pogell, B. M.: Serum Protein Changes in Diabetic Retinopathy, read before the Eastern Section Meeting of the Association for Research in Ophthalmology, New York, April 28, 1956.

‡ Lerman, S., and Pogell, B. M.: Serum Protein Changes in Diabetic Retinopathy, read before the Eastern Section Meeting of the Association for Research in Ophthalmology, New York, April 28, 1956.

§ References 19-23.

‖ Naquin, H. A.: Personal communication to the author.

¶ Reference 5; Hoover, R.; Becker, B., and Winter, F.: Data presented at Wilmer Resident's Meeting, Johns Hopkins Hospital, 1953.

References 5 and 28-32; Winter, F.: Data presented at Wilmer Resident's Meeting, Johns Hopkins Hospital, March, 1953.

Hypophysectomy Versus Adrenalectomy

Hypophysectomy removes the source of corticotropin and causes adrenal atrophy and hypofunction. Why is hypophysectomy preferable to removing both adrenals? The completely adrenalectomized patient, without any mineralocorticoid hormone (probably aldosterone from the zona glomerulosa) easily goes into electrolyte imbalance and shock without adrenal replacement therapy. Maintenance after hypophysectomy is safer. A relative depression of the zona fasciculata, which is suspected of hyperactivity in retinopathy, theoretically should be accomplished with relative sparing of the zona glomerulosa. Also, the required cortisone maintenance dose tends to be lower after hypophysectomy than after adrenalectomy. If glucocorticoids help cause retinopathy, hypophysectomy should be preferable because of the smaller steroid replacement need.

Evidence that hypophysectomy exerts its adrenal depressive effect mainly on the zona fasciculata is as follows: Experimentally, in various animals after hypophysectomy, atrophy occurs in the zona fasciculata but not the zona glomerulosa.* These experimental animals show apparently normal or nearly normal zona glomerulosa function, with no fatal electrolyte imbalance. Clinically, patients with hypopituitarism show depressed zona fasciculata function but no marked electrolyte imbalance.[37] Posthypophysectomy patients have been reported to show low zona fasciculata function by reduced ketosteroid excretion and poor adrenal response to corticotropin,† but they have very little electrolyte imbalance. The cases of hypophysectomy in our series have had no electrolyte imbalance even when tested by a low-salt diet without cortisone therapy. From autopsy studies in the Henry Ford Hospital on patients who had had hypophysectomy performed for metastatic malignancy, atrophy of the zona fasciculata was found along with some generalized adrenal atrophy.

Effectiveness of Hypophysectomy in Humans

The likelihood of an incomplete hypophysectomy and its effectiveness should be mentioned. Hypophysectomy can be complete, as was found at autopsy by serial sections of the sella in one case of postoperative hypophysectomy in Luft's series[2]; also, one case in our cancer series had no pituitary remnants, as demonstrated by histological sections. Another case in Luft's series had some pituitary remnants.[2] Five of six cases in our cancer series had pituitary remnants on histological sections of the sella. Three of these cases with pituitary remnants had adrenal cortical atrophy. Histological atrophy of the thyroid was found in two cases, and the gonads were atrophied histologically in one case (Table 1). The other patients had no thyroid tissue taken or had been castrated previously for their metastatic malignancy or had died too shortly after hypophysectomy; so no changes in these organs could be expected. Although hypophysectomy is not always total, this suggests that hypophysectomy is usually effective enough to induce some atrophy of the organs dependent on trophic hormones of the pituitary. However, there is evidence to indicate that adrenal function is usually the last to fail. Clinically, patients after hypophysectomy in our series and in Luft's series usually developed low urinary ketosteroids, suggesting reduced function of the gonads and the adrenal zona fasciculata. In our series, the urinary 17-hydroxysteroids were not consistently lowered following hypophysectomy.

* References 33-36.

† References 2 and 3.

TABLE 1.—*Results After Hypophysectomy for Malignant Disease*

Case No.	Weeks Postop.	Adrenal Autopsy	Studies 17-OHS	17-KS	Thyroid	Gonads
1	7	Atrophy			Atrophy	Atrophy FSH 4-8 m.u.
2	0		23.8			
	2		7-12	3-7		
	26	Atrophy			Atrophy	Castrated
3	2½	Atrophy			N.D.	Castrated
4	1		19.4	5.8	B.M.R. −27%	
	25		24.8	6.6	I^{131} 2%	
	60			3-7		FSH 4 m.u.
5	0				B.M.R. +13%	
	36		3.6	12.5	B.M.R. −10%	
	52		17-30	4.5	B.M.R. −19%	
6	0		28.4			
	3		8.2			
	10			3.1	Clinically	
	30			2-7	hypothyroid	
	56		31.4	3.4		

Because of the loss of thyroid-stimulating hormone, a low B.M.R. developed and radioactive iodine uptake was greatly reduced. Sensitivity to administered insulin was increased, probably owing to removal of the diabetogenic influence of the pituitary. The blood pressure was usually reduced.

Other Evidence Suggesting Hypophysectomy For Diabetic Retinopathy

The effectiveness of hypophysectomy in causing adrenal atrophy, and the reasons why this might favorably influence diabetic retinopathy, have been reviewed. Another possibility is that the pituitary itself may be the direct cause of diabetic retinopathy. Adrenal hyperfunction in diabetic retinopathy may be merely secondary to a basic pituitary hyperfunction. Experimentally, there is much evidence to indicate the possible importance of the pituitary in the etiology of diabetes. For example, Lukens has produced experimental pituitary diabetes in dogs by a short course of pituitary extract, and yet the diabetes produced was permanent. In the late or permanent stage there is little or no evidence of pituitary hyperactivity in such an animal. It is possible that pituitary overactivity may initially help cause diabetes without continuing throughout life.[38] Lukens and Dohan showed that a long course of anterior pituitary extract would produce Kimmelsteil-Wilson lesions as well as diabetes in the dog.[39] Kimmelsteil-Wilson lesions can also be produced by cortisone. However, the typical aneurysms of diabetic retinopathy have not been found in animals given cortisone.‡ Neither was any evidence of diabetic retinopathy found in dogs treated with anterior pituitary extract by Lukens and Dohan.§ However, flat preparations of the retina were not made in these cases.‖ (At the Henry Ford Hospital under the direction of Dr. Oliver Gaebler, a depancreatized dog has been kept

‡ Rosen, D. A.: Data presented at Wilmer Resident's Meeting, Johns Hopkins Hospital, April, 1954.

§ Leopold, I.: Personal communication to the author.

‖ Leopold, I.: Personal communication to the author.

under growth hormone for the past two years. No signs of diabetic retinopathy can as yet be seen ophthalmoscopically in this animal.¶)

Another factor is the antagonistic effect of pituitary growth hormone and insulin. For example, the depancreatized cat requires 10 to 20 units of insulin a day, while the depancreatized and hypophysectomized "Houssay animal" requires only ½ unit a day for equally good maintenance.[38] There is experimental work indicating that pituitary growth hormone stimulates and eventually destroys the islets of Langerhans in dogs.[38] Fat synthesis in the experimental animal, which is upset by removing the pancreas, is restored by also removing the pituitary.[38] Clinically, acromegaly with its apparent hypersecretion of growth hormone is accompanied by outright diabetes in 17% of the cases, and 30% show some disturbance in carbohydrate metabolism.[38] I have already mentioned instances of spontaneous pituitary atrophy and termination of pregnancy as improving the course of diabetic retinopathy. Thus, it is possible that pituitary hyperfunction may cause diabetes in a susceptible person, and pituitary function may then return to normal without causing vascular complications. It is conceivable that is some cases pituitary hyperfunction might continue, and this might lead to vascular complications. These vascular complications could be the combined long-term effect of pituitary lipotrophic hormone, growth hormone, and corticotropin-induced adrenal hypercorticism with any or all of these combined effects on carbohydrate and protein and lipid metabolism.

In summary, then, hypophysectomy can be rationalized as a possible treatment for preventing progress of diabetic retinopathy from the standpoint of either a direct effect or a secondary hormonal effect, or both.

Mortality Rate From Hypophysectomy

In recent years, diabetic nephropathy has caused an increasing percentage of the deaths in juvenile diabetics. In the period 1922 to 1936 diabetic nephropathy caused only 2% of the deaths in patients with onset of diabetes under the age of 15 years. In the period 1937 to 1943 this jumped to 12%; in the period 1944 to 1949 this jumped to 36%, and in the period 1950 to 1953 nephropathy caused 63% of the deaths. Thus, patients with severe diabetic retinopathy and severe Kimmelsteil-Wilson disease are seriously threatened with death as well as with blindness. In many of the reported cases hypophysectomy in diabetics has been performed for nephropathy rather than for retinopathy.# However, we must remember that there is a definite mortality rate associated with hypophysectomy itself. The operative mortality rate occurring within a week or two of

TABLE 2.—*Mortality from Hypophysectomy*

A. For metastatic malignancy	
70 cases (Bronson Ray)	
3%-5% est. operative mortality	
10% total mortality (30 days)	
B. In Diabetes	
1. 20 cases (Luft)	
10% operative mortality	
25% total mortality (6 mo.)	
2. 5 cases (present study)	
0 mortality to date	

¶Schimek, R. A.: Unpublished data.

References 2 and 3.

* Ray, B.: Personal communication to the author.

hypophysectomy was estimated to be only 3% to 5% in 70 cases done for metastatic malignancy by Bronson Ray,* and it was 10% in the 20 cases done for diabetic vascular complications by Luft.[2] The percentage mortality from all causes, occurring within one to six months of the operation, was 10% and 25%, respectively (see Table 2). There have been no deaths in the five cases of hypophysectomy for diabetic retinopathy reported in this communication. These five cases are reported here.

Report of Cases

A 32-year-old white woman had been diabetic since age 3. The patient had had neuropathy and nephropathy, with Kimmelsteil-Wilson syndrome, hypertension, and a history of progressive loss of vision for two years, with hemorrhages, exudates, and early retinitis proliferans in both eyes. Hypophysectomy was performed in July, 1955. During the nine months following operation the insulin requirement has been cut to one-third and blood pressure has dropped close to normal levels. Symptoms of hypothyroidism are controlled by ½ grain (30 mg.) of thyroid per day. Albuminuria has almost cleared, and red cells in the urine have disappeared. Vision in both eyes has remained about the same

TABLE 3.—*Results of Hypophysectomy in Patient 1*

	Preop.	9 Mo. Postop.
Insulin	42 u. lente	15 u. lente
Av. B.P.	190/110	140/95
Thyroid	B.M.R. +7%	30 mg. thyroid q.d.
Albuminuria	++to+	Tr.
RBC, urine	2-25 RBC	0
Vision R.E.	C.F. at 1 ft.	C.F. at 2 ft.
Vision L.E.	20/300	20/300
Hemorrhages	Many	Essentially cleared
Exudates	Many	Same
Proliferans	Early	Same
17-ketosteroids		6.5 mg.-5.9 mg.
FSH		Less than 4 m.u.u.
17 (OH) steroids		17.1 mg.

(Table 3). The exudates and retinitis proliferans have remained unchanged. The hemorrhages have seemed to clear remarkably, with all of the vitreal and retinal hemorrhages clearing completely and not returning during this period. The 24-hour urinary 17-ketosteroids are only slightly lowered, to 5.9 mg. The patient is now maintained on 10 mg. of hydrocortisone twice a day. The patient had had a recurrent infection of the foot, which recurred postoperatively and required extensive debridement six months after operation.

A 54-year-old white man had severe diabetes and minimal signs of Kimmelsteil-Wilson syndrome. There were hemorrhages, exudates, and retinitis proliferans in both eyes. Loss of vision and retinopathy progressed despite therapy with carbazochrome (Adrenosem), testosterone, and cyanocobalamin. Hypophysectomy was performed in September, 1955. During the seven-month postoperative period the insulin requirement and blood pressure have remained lowered. Postoperatively, the radioactive iodine uptake shows greatly reduced thyroid function. Symptoms of hypothyroidism are controlled by ½ grain of thyroid every day. Although the vision was 20/80 in the left eye preoperatively, when first checked postoperatively it was 20/200. Since then, vision in both eyes has remained the same (Table 4). The exudates have remained the same in both eyes, as has the proliferans formation. The hemorrhages have partially cleared. A two-day trial without salt and without corticosteroid replacement therapy

TABLE 4.—*Results of Hypophysectomy in Patient 2*

	Preop.	Postop.
Insulin	35 u. PZI	20 u. PZI
Av. B.P.	150/70	105/70
Thyroid		I^{131} at 6 hr.: 17%; with TSH 40%
Vision R.E.	20/300-20/200	20/200+1
Vision L.E.	20/80-20/70	20/200
Hemorrhages	Many	Improved
Exudates	Many	Same
Proliferans	Moderate	Same or improved
Ketosteroids		2.8 mg.
17 (OH) steroids		21.4 mg.
PSH		4-8 m.u.u.

showed no signs of electrolyte imbalance; this suggests continued function of the salt-regulating zona glomerulosa. Urinary ketosteroids have been very low, 2.8 mg., indicating reduced gonadal and adrenal function. The patient is maintained on 5 mg. of prednisone (Meticorten) twice daily.

A 35-year-old white man had had known diabetes since age 3 and had taken insulin continuously since age 5, with poor control. There was retinopathy with hemorrhages, exudates, and proliferans, with no albuminuria and no hematuria but slight reduction of urea clearance. Loss of vision and retinopathy progressed despite treatment with x-ray, a preparation of hesperidin and ascorbic acid (Hesper-C), a trypsin preparation (Parenzyme), rutin, and ascorbic acid. In November, 1955, hypophysectomy was performed. During the six months following operation, insulin requirements and blood pressure have been reduced. The B.M.R. has fallen to − 28%. Urea clearance and phthalein excretion have continued about the same. Vision in the right eye has improved from light perception to counting fingers, mainly because of clearing of hemorrhages, and vision in the left eye has remained about the same. The hemorrhages have been slowly clearing in both eyes, but the exudates and proliferans have appeared to remain stationary. After hypophysectomy, urinary corticosteroid levels were lowered, with a low response to corticotropin. The patient is maintained on 12.5 mg. of cortisone twice a day (Table 5). Several months postoperatively an appendec-

TABLE 5.—*Results of Hypophysectomy in Patient 3*

	Preop.	Postop.
Insulin	40 isophane+10 u. CZI b.i.d.	34 u. isophane
Av. B.P.	154/90	90/70
Thyroid		B.M.R. −28%
Urea clearance	81. lowered	Same
Phthalein excretion	61% (2 hr.)	65% (2 hr.)
Vision R.E.	L.P.	C.F.
Vision L.E.	C.F.	C.F.
Hemorrhages	Severe	Improved
Exudates	Severe	Same
Proliferans	Moderate	Same
17 (OH) steroids	9.4 mg.	2.8-8.0 mg. with corticotropin 18.1 mg.

tomy was necessary, and the patient also developed a transient pyelonephritis, which cleared uneventfully.

Quite recently a fourth patient with diabetes with microaneurysms, hemorrhages, and exudates in both eyes but without any retinitis proliferans, and with rather severe Kimmelsteil-Wilson syndrome, has had hypophysectomy. This patient had a much earlier stage of diabetic retinopathy, with 20/30 vision in each eye, and the chief indication for hypophysectomy was the severe Kimmelsteil-Wilson syndrome. Postoperative recovery appears to be proceeding uneventfully,

but insufficient time has elapsed since operation to observe an effect on the retinopathy. The follow-up of this case, and of subsequent ones without irreversible changes such as retinitis proliferans, in time should permit evaluation of any markedly beneficial effect hypophysectomy might have on diabetic retinopathy.

A patient of Dr. Frank Walsh who had diabetic retinopathy and who was subjected to hypophysectomy several months ago at the Johns Hopkins Hospital is herewith reported as the fifth case, with Dr. Walsh's permission. In one eye, hemorrhage has cleared so that vision has improved from counting fingers to 20/25. Vision in the other eye has remained 20/40.

Summary

Adrenal and pituitary factors in diabetic retinopathy suggest that hypophysectomy may be of value. Following hypophysectomy, five diabetics with retinopathy have, at least for the time being, stopped losing vision and having severe repeated hemorrhages in the retina. These could very well be simple spontaneous remissions. These reported cases are too few, with the follow-up too short or the retinopathy too advanced, to decide whether hypophysectomy is beneficial. While hypophysectomy is a formidable procedure, with some 5% to 10% mortality, further trial appears indicated.

The treatment of the patients whose cases are reported herein, and their selection for hypophysectomy, has been a joint endeavor of Drs. Richmond Smith, William Lowrie, Robert Knighton, John Bryan, Earl Redfern, Raymond Mellinger, Fred Whitehause, William Willoughby, David Barsky, and myself, carried out in the Departments of Endocrinology, Metabolism, Neuro-Surgery, and Ophthalmology of the Henry Ford Hospital.

Addendum

On subsequent follow-up, the first, third, and fourth patients (now 13, 10, and 6 months after operation, respectively) have maintained the same vision, with some fundus improvement as regards hemorrhage. The second patient (now 11 months after operation) recently had visual improvement in the right eye to 20/70—2, but visual loss in the left eye to counting fingers with very little change in fundus appearance. The fifth patient (Dr. Walsh's) has continued to have improvement of vision from counting fingers to 20/25 (R.E.) and from 20/40 to 20/30 (L.E.).

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The Continuous Edge-to-Edge Suture in Full-Thickness Corneal Grafts

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In full-thickness keratoplasty, with cylindrical graft, the majority of the mechanical postoperative complications are consequences of bad coaptation of the graft, due to some defect in the section or in the fixation. The use of instruments of first quality and the edge-to-edge suture have nearly eliminated them.[1]

At first fixation was accomplished in 4 mm. grafts by using the sharp and very polished Vogt's suture needles, manufactured by Grieshaber and threaded with 000000 silk; placing two points at the extremes of the vertical meridian and progressively increasing its number until they are equal or even superior to the number of millimeters of the diameter of the graft.[2]

The "sharp side," on Vogt's needle, has been modified to place it in the convexity, in order to safeguard the bridge of the tissue at each side of the wound,[3] which is attempted to be joined with the suture, making it easier to place the stitches nearer each other. The number of stitches was limited for fear of traumatizing the graft by the irritation which the knots and ends of silk would cause. The suture of pure silk of seven strands, 0.04 mm. thick, was well tolerated by the tissues and allowed us to increase the number of stitches to 16 in grafts of 6 mm. and to 32 in large grafts. The toleration of this material is due not only to its thinness but also to the absence of any chemical substances in it.

With this multiple suture displacements of the graft and ruptures of the wound disappeared. This allows the patient freer movements and a shorter time in bed and necessitates a binocular dressing only for a few hours after the operation, until the effect of the anesthesia and premedication disappears, allowing the patient a convalescence at home after the first change of dressings. This dressing is performed on the second or third day.* The main purpose of the first dressing is to check on the formation of the anterior chamber.

The advantages of this firm closure of the wound are offset somewhat by irritative disturbances produced by the sutures, which are far less with pure silk than with 000000 silk. But these disturbances are more evident in patients with a monocular bandage leading an ambultory life than in patients with a binocular dressing who remain in bed.

The stitches placed in the cornea act as foreign bodies and produce pain and irritative reactions. The objective manifestations of such irritation are palpebral edema, blepharospasm, photophobia, perikeratic hyperemia, difficulty in dilating the pupil, and, posteriorly, formation of new corneal vessels. A retrobulbar anesthetic injection at the time of operation of sufficient alcohol to obtain a concentration of 10%-20% prevents such trouble in many cases. A higher concentration can not be recommended for fear of orbital edema.[3]

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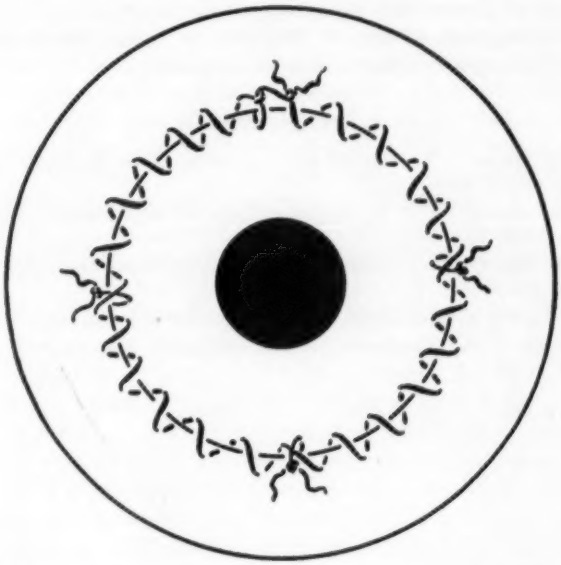
* Rycroft,[4] p. 96.

To remove the stitches is a delicate operation that must be performed by the surgeon himself under magnification. If this is done 15 days after operation, some opening of the wound, accompanied by flatness of the anterior chamber and partial ectasia of the graft, can frequently be observed. Leaving the total number of stitches for 20 or 25 days is annoying to the patient and did not avert the risk of opening the wound when all the stitches were removed simultaneously. For this reason, we decided to remove the stitches in a progressive way, doing it on three different days at eight-day intervals, beginning 8 or 10 days after surgery and removing every second stitch.

This technique proved satisfactory, especially in keratoconus, in which healing is slower and therefore the tendency toward opening of the wound and ectasia is greater.

To reduce the discomfort of the patient, we tried a continous suture beginning at a point placed at the 12 o'clock position. Two previous discontinuous points, at the extremes of the vertical meridian, or four points, at the 12, 3, 6, and 9 o'clock positions, facilitate the location of this suture. The previous stitches are also useful for fixation when the continuous suture is removed (Figure).



The number of stitches can be equal to, and even greater than, that in the discontinuous suture, even reaching the number of 25 in a graft of 7 mm. and in this way increasing the firmness of the fixation and the coaptation of the graft. Also, a better apposition of the epithelial and endothelial planes is obtained, due to the oblique course of the silk between two points, acting as a bridge suture to the epithelial layers. We have used pure silk of seven strands, but 000000 silk can be used.

Sharp needles with the cutting edge at the convexity are used to avoid union between two adjacent points and the tearing of the bridge of the tissue to be joined with the suture. The dimension of the needle can be 4 to 5 to 7 mm., depending on the skill of the surgeon.

The suture forceps must be very fine to allow the location of stitches sufficiently near each other without difficulty and with a minimum of traumatism for the graft. The needle holder will depend on the dimension of the needles used.†

With this technique postoperative troubles diminished considerably and the patient's use of the eye not operated on becomes possible and more efficient. The continuous suture is removed at the 10th or 20th day. For this purpose it is enough to cut the thread every third loop and pull it up from the central one. The previous points must remain till the 30th day in keratoconus and other processes of slower healing, to avoid the rupture of the wound. The best instrument for this purpose is Schaaf's forceps and a fragment of a razor blade held in a needle holder.[5] Control with the surgical microscope is desirable and a magnifying glass at least indispensable.

Summary

In full-thickness keratoplasty, the multiple suture—edge to edge—with pure silk, with the progressive removal of the stitches under control of a magnifying glass, or the use of a continuous edge-to-edge suture is advised.

Retrobulbar injection of alcohol 10%-20% to reduce the irritative reactions produced by the corneal stitches is also recommended.

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† Rycroft,[4] p. 231.

Electron Microscopy of Trachoma Virus in Section

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The trachoma virus, Chlamydozoon trachomatis, can be found as epithelial inclusion bodies in conjunctival scraping slides. The morphology of the virus in scraping smears has been well established. However, the morphology of the virus in sections still stands on rather slender experience. Knowledge of the micromorphology of inclusions as obtained by the electron microscope is very limited. Some experiments have been reported on the electron microscopy of this virus. Most of them have been performed, however, with a purified virus. One of us (Y.M.) studied the same subject with Tsutsui and Tanaka in 1952.[1] It was supposed from the experiment with purified virus that trachoma virus might have microstructures, details of which, however, were not solved by an experiment with purified virus. Electron microscopy of trachoma virus in section thus warranted attention. It was also necessary to carry out this investigation as a basic study of trachoma virus cultivation by tissue culture technique, which we have in progress at present, under the support of the National Council to Combat Blindness, Inc.

Method

So far the trachoma virus has not been cultivated in vitro; the material of the present study was obtained from patients.

Selection of Patients.—By repeated field examinations, trachoma cases with clinical appearance of Tr. FP (inclusions) * were selected. The standard for the 3+ inclusions was at least 50 epithelial cells with inclusions in one scraping slide. Twelve such cases were obtained for the present study.

Resection of Conjunctiva.—The resection of conjunctiva was performed, particularly in chronic-stage cases, at least two weeks after the scraping examination, because immediately after a scraping examination there was a lessening of inclusions. In acute-stage cases, however, such a long delay was not required.

A spindle-shaped piece of conjunctiva was cut from the upper fornix of each case. No irrigation of the eye was done before operation. The conjunctiva was cut, after a subconjunctival injection of procaine solution, by one stroke of the scissors without using forceps. Infection was prevented by giving antibiotics topically and systemically after operation. These pre-

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* WHO classification of trachoma.

cautions seem to be important for histological demonstration of inclusions. Most of the inclusion bodies are found, as will be discussed later, in the superficial layers of conjunctival epithelium. The epithelial cells with inclusions are extremely loosely attached to the underlying tissues. They are easily released from the latter by a slight force applied to the epithelial surface.

The piece of conjunctiva was then placed on a filter paper, epithelial side up. With small forceps, it was stretched on the paper by holding the margins. The piece then measured about 6×20 mm. It was then cut into two pieces at the middle of the longer diameter with sharp scissors. One-half of the piece was dipped into 10% formalin for ordinary histological study. The second half was fixed with 1% buffered osmic acid for electron microscopy.

Examination by Light Microscope.—The first half of the tissue was fixed in formalin for a few hours. Ordinary paraffin sections of 5μ thick were then prepared. The general histological structure was examined by such routine stains as hematoxylin and eosin (Fig. 1). Examination for inclusion bodies was made after staining with the Giemsa method and differentiation with acetone (Figs. 2, 3, and 4). Some other stains, such as methyl green-pyronine, thionine, and iodine, and examination with the phase-contrast microscope were employed as well.

The purpose of this examination was twofold. The first was to select more suitable cases for electron microscopy. Among 12 cases selected by clinical examinations, 2 were thus proved to be the best material for electron microscopy: 1 case of acute trachoma, of one month's duration, and 1 case of chronic trachoma, of six months' duration. In both these cases 30 to 50 inclusions were demonstrated in every section about 6 mm. long. The distribution of the inclusions was so diffuse that the bodies were found along the epithelial layer in almost all fields of immersion microscopy. These cases were thus selected to be the main subject of the present study. In other cases the distribution of the inclusions was rather biased.

The second purpose was to study the inclusion morphology in sections by the light microscope. This study constitutes a basis for electron microscopy and will be discussed again later.

Examination by Electron Microscope.—The second half of the tissue was fixed with 1% buffered osmic acid solution for 30 to 120 minutes in a refrigerator. After the fixation, the piece of tissue was again cut with a razor blade into slender pieces, of about 1 mm. width, without separation from the filter paper. Further manipulations were as follows:

1. The tissue was gently washed with six changes of purified water, with 10 minutes in each change.

2. It was dehydrated with two changes each of 70%, 90%, 95%, and 100% alcohol, 30 minutes in each change.

3. The pieces were dipped in a mixture of 100% alcohol and a monomer † (1:1) for one hour at room temperature.

4. They were placed in the first change of monomer for one hour and in the second change for one night in a refrigerator.

† The monomer employed was a mixture of refined N-butylmetacrylate and methylmetacrylate, 100:15.

5. The tissue was embedded in a mixture of monomer and benzol peroxide (100:3), at 45 C. It took 6 to 24 hours for polymerization to be completed.

Just before the embedding, the tissue was separated from the filter paper, which indicated the opposite side of the epithelium. Then a small stopper of filter paper was put at one end of the slender piece of tissue in order to hang the latter in an embedding capsule. The epithelial side of the tissue was marked on the stopper.

After the completion of polymerization, the tissue was cut into thin sections by a rotary ultramicrotome ‡ of Spencer type. The deeper layers of conjunctival tissue were cut off with a razor blade before sectioning except for the purpose of subepithelial examination. The sections were then examined with the Akashi-TRS-50B § electron microscope. This microscope was easy to operate, and highly efficient. We were able to operate the microscope without assistance of technicians.

The embedding material, acryl resin, was not removed by a solvent such as amyl acetate before microscopy. It was removed through sublimation by the electronic ray during the observation.

Results

Findings with the Light Microscope

With the light microscope inclusion bodies are found, as is well known, exclusively in the epithelial layer of the conjunctiva, particularly in the superficial layer. In acute-stage cases they are also found in a relatively deeper layer of the epithelium; nevertheless, the basal layer of the epithelium has no inclusions in general.

When paraffin sections are stained with the Giemsa method and differentiated with acetone, the best morphology of the inclusions is obtained. An intensive staining of inclusions is obtained also with the methyl green-pyronine or with the thionine stain, but these stains give poorer morphology than does the Giemsa stain. Hematoxylin gives a faint stain but a clear morphology. However, when the tissue is stained with eosin after hematoxylin as a routine histological method, a discoloration of the inclusions occurs.

A diffuse distribution of inclusions is found in the acute- and early-chronic-stage cases. In most chronic cases of advanced stages, inclusions are apt to be grouped to form nests; thus, a bias of the distribution results. For this reason, 3+ inclusions in the scraping alone do not necessarily indicate an easy demonstration of inclusions by the electron microscope in sections.

Corresponding to the sites of positive inclusions there are destructive inflammatory changes in the epithelium. These changes are an edematous swelling and looseness of epithelial cells with cellular infiltration into the epithelial layer. These changes are often so striking that not even a trace of the original structure of the epithelium is observable. Intensive subepithelial changes, such as follicle formation and cellular infiltration, are found corresponding to the nests of inclusions (Fig. 1). Proliferation of the epithelium is never found at the site of inclusions.

‡ Product of the Nihon Microtome Co., Ltd., Osaka, Japan.

§ Product of Akashi Seisakusho, Ltd., Tokyo.

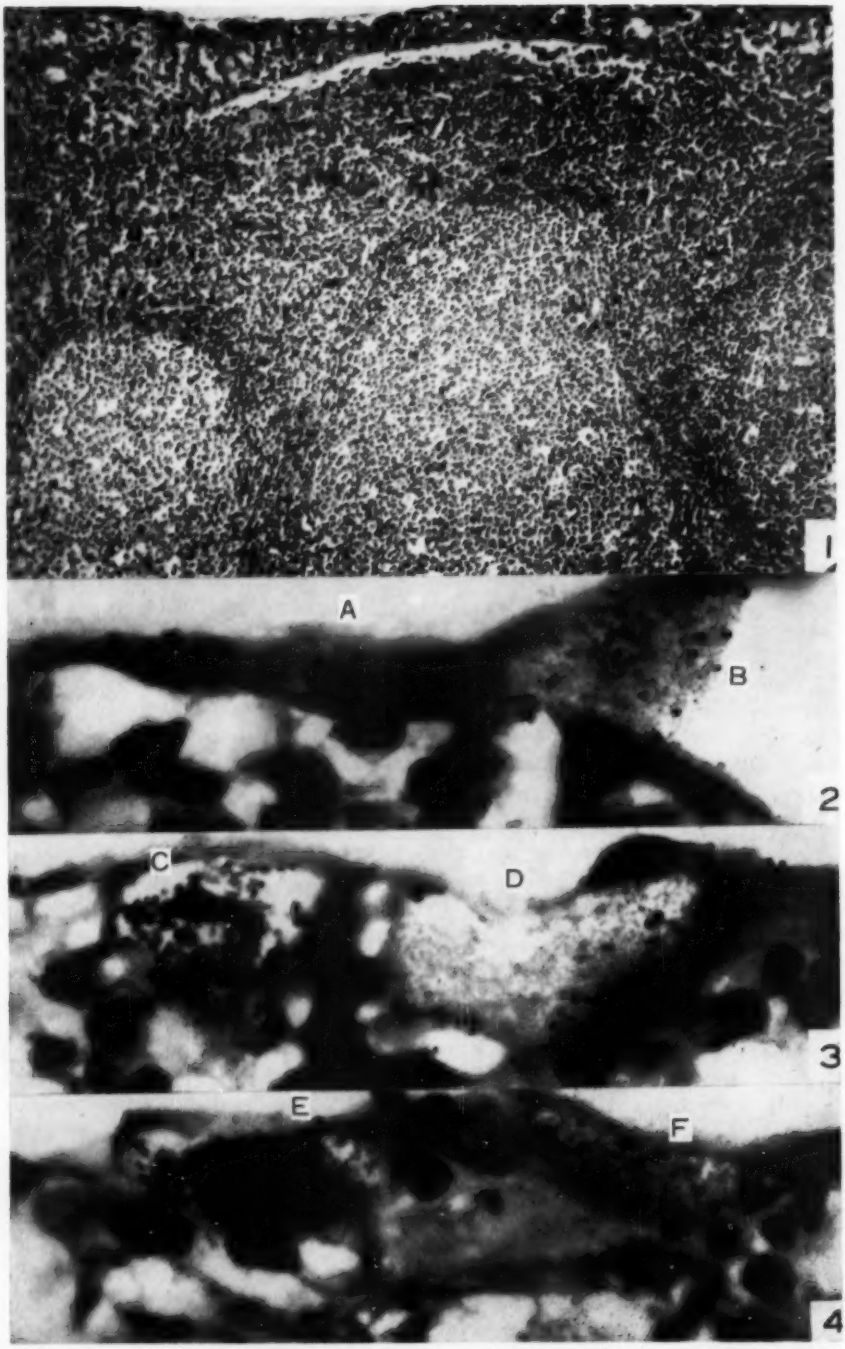


Fig. 1.—Ordinary histology of trachomatous conjunctiva, a chronic case of six months' duration. A destructive, inflammatory change of the epithelial layer, with intensive infiltration and follicle formation in subepithelial tissues, is obvious. Hematoxylin-eosin stains.

Figs. 2, 3, and 4.—Epithelial inclusions in paraffin sections, as seen by a light microscope; same case as that in Figure 1. Giemsa stain. *A*, a pure initial-body inclusion without distinct inclusion cavity. *B*, an "elementary-body inclusion," which may be mature. A small number of initial bodies are seen with a predominance of elementary bodies. *C*, an initial-body inclusion in a distinct cavity. *D*, an elementary-body inclusion, which may be hypermature. *E* and *F*, elementary-body inclusions, which may be young.

Most inclusion bodies are found in a cavity of epithelial cytoplasm, the inclusion cavity. In general, inclusion bodies in larger cavities consist of elementary bodies (Figs. 2*B*, 3*D*, and 4). Inclusion bodies in smaller cavities consist of initial bodies. In some pure initial-body inclusions, a distinct inclusion cavity is hardly recognizable, even by examination of serial sections (Fig. 2*A*).

Most "elementary-body inclusions" contain a varying number of initial bodies besides a large number of elementary bodies. Therefore, they actually consist of a mixture of elementary bodies and initial bodies. In general, the "elementary-body inclusions" are predominant, and pure initial-body inclusions are few in number. Only in the acute stage is the proportion of the pure initial-body inclusions very high.

Initial bodies stain intensively by the Giemsa method, having a bluish or violet tint. The color tint of elementary bodies varies greatly, probably being related to the developmental stage of the virus. Some of them stain violet, like initial bodies. These may be young elementary bodies (Fig. 4*E*). Others stain reddish, and they may be mature (Figs. 2*B* and 4*F*). Some elementary bodies stain faintly rose; they may be hypermature or degenerative (Fig. 3*D*).

Inclusion bodies are often embedded in an amorphous ground substance as seen with the Giemsa stain. In some inclusions the ground substance covers the inclusion bodies so intensively that the latter are often not clear, but are stained as a group.

With iodine, inclusion bodies are seen to be embedded in an amorphous ground substance stained with iodine, which was first demonstrated by Rice[2] in scraping material and termed carbohydrate matrix. The matrix substance varies greatly in intensity according to the inclusions. It may sometimes be absent.

The only finding to be differentiated from inclusions in section is mast-cell granules. Mast cells are found in the deeper layer of the subepithelium. Mast-cell granules are found in the cytoplasm itself and not in a cavity. They are larger than elementary bodies in general and have a different color tint. They never have a carbohydrate matrix.

With the Poleff method,[3] mast-cell granules are stained intensively, while actual inclusion bodies in the epithelium do not stain with it.

Findings with Electron Microscope

1. *Typical "Elementary-Body Inclusions."*—A fully developed, typical "elementary-body inclusion," when examined at a lower magnification by the electron microscope, has a morphology entirely corresponding with that seen with a light microscope, particularly with that in scraping specimens. (Fig. 5IB_4 and IB_5 and Fig. 7). Therefore, there is no difficulty in the identification.

The inclusion bodies are found in a cavity in the cytoplasm of epithelial cells. The inclusion cavity occupies a large part, sometimes almost the entire space, of the cytoplasm. The nucleus of the cell is pushed toward one side in a crescent form. Nevertheless, a degenerative change in the nucleus is seldom met with.

The inclusion cavity is sharply defined. There is sometimes a vacant

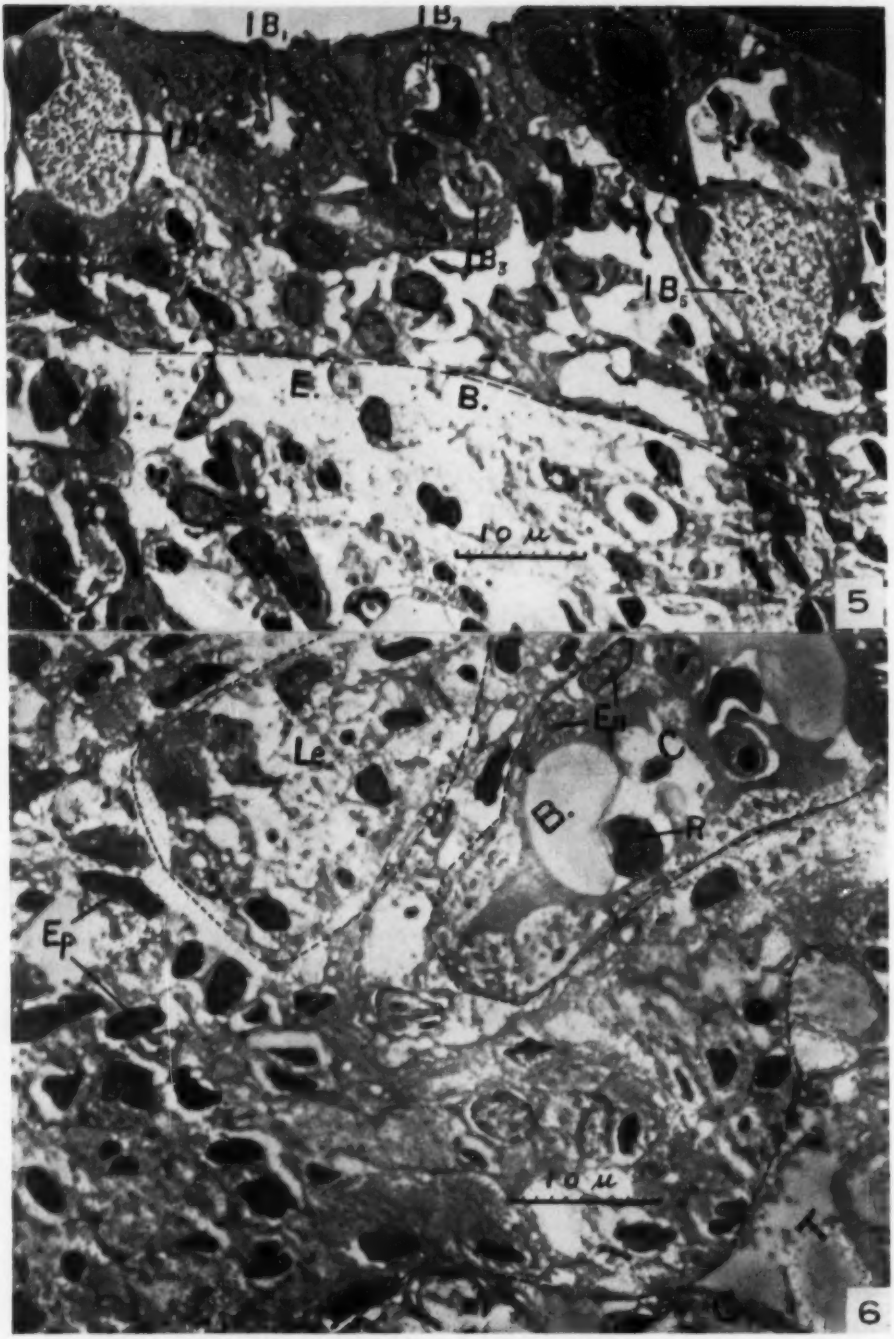


Fig. 5.—General histology of superficial conjunctiva in trachoma as observed by an electron microscope. × 2080.

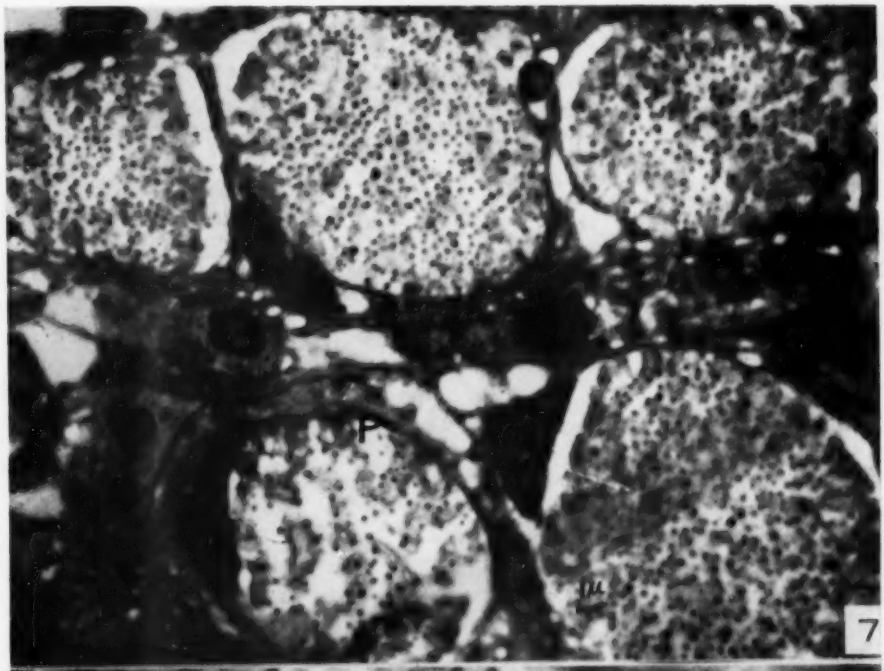
IB$_1$, *IB*$_2$, and *IB*$_3$, inclusions of relatively early stage.

IB$_4$ and *IB*$_5$, fully developed elementary-body inclusions.

E.B., epithelial border line, indicated by a dotted line.

Fig. 6.—A deeper layer of trachomatous conjunctiva as seen by an electron microscope. × 2300.

Ep, epithelioid cell; *B.C.*, blood capillary; *R*, red blood cell; *Le*, Leber cell; *En*, endothelial cell of capillary wall; *C.T.*, connective tissue of tunica fibrosa.



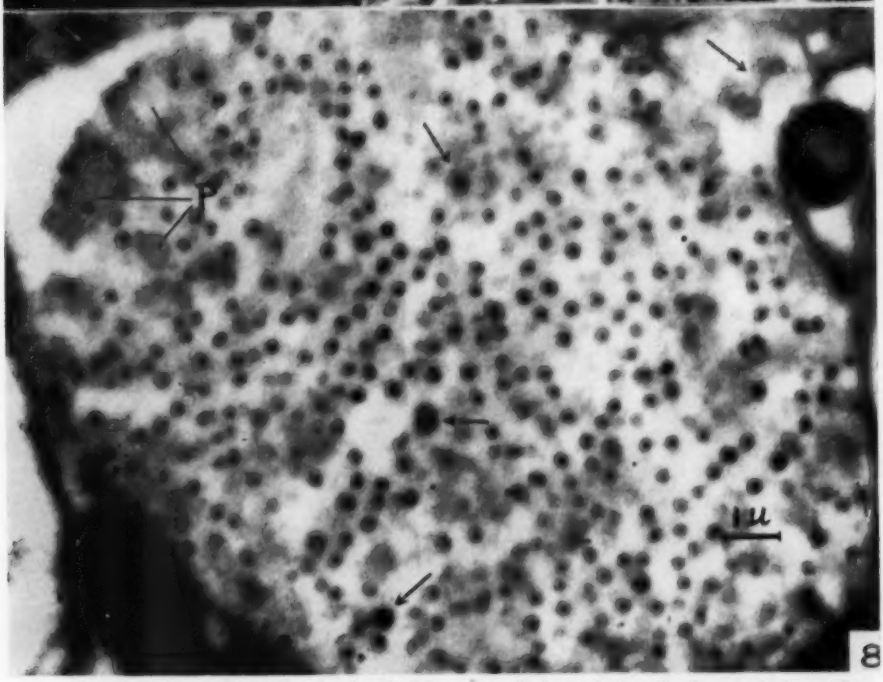
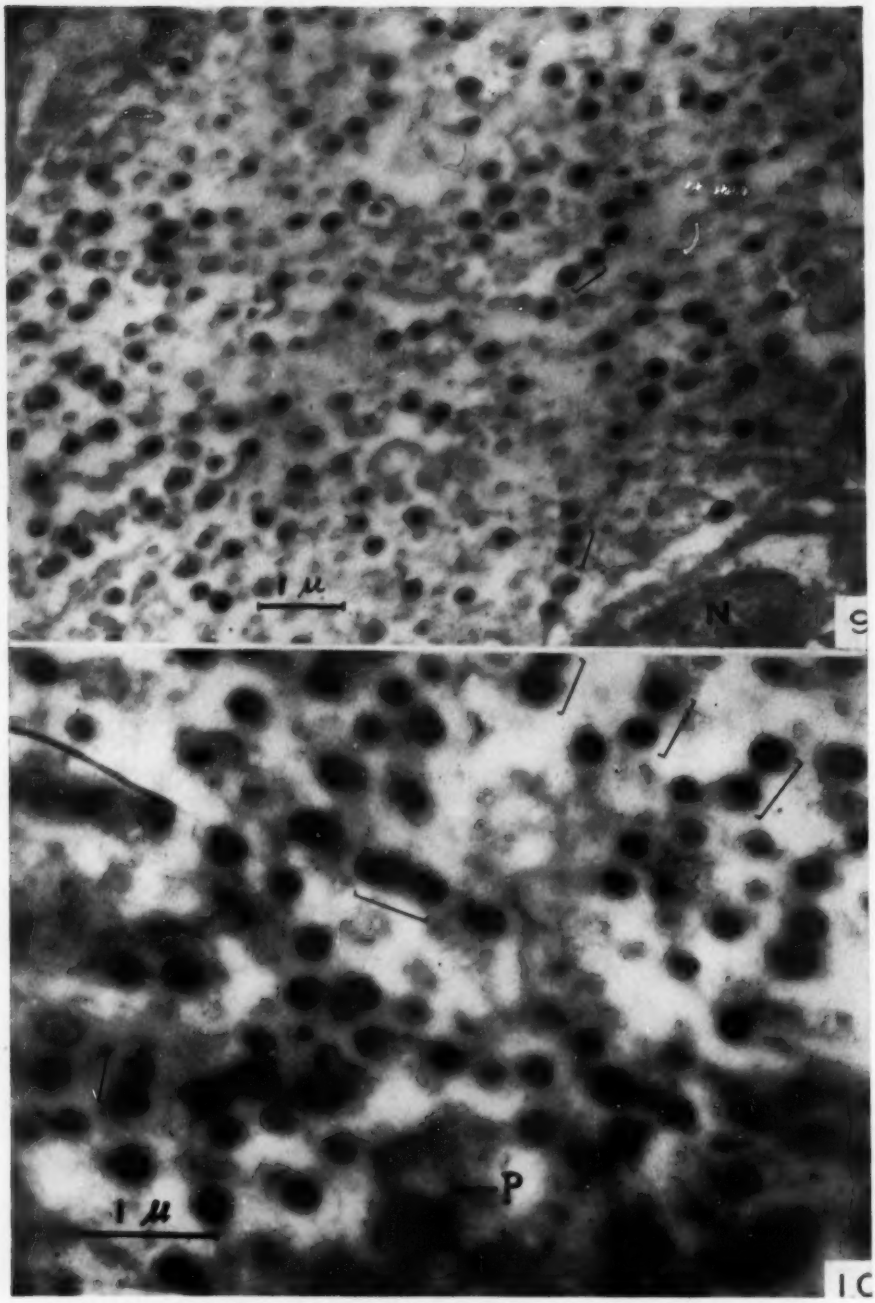


Fig. 7.—A nest of fully developed "elementary-body inclusions." One inclusion (*P*) seems to be in an earlier stage, having huge "polygons," which might be a vegetative form of C. trachomatis. × 3500.

Fig. 8.—A high magnification of the middle and upper inclusion in Figure 7. Granules of 200-350 mμ are predominant. Some of them have a very dense central granule. A sphere membrane 400-500 mμ in diameter is apparently surrounding many of the granules. There are some large dense granules as indicated by arrows, which may correspond to the initial body seen by a light microscope. Suspicious appearance of "polygons" at the marginal portion of the inclusion (*P*). × 9000.



Figs. 9 and 10.—Fully developed "elementary-body inclusions" at high magnifications. Various forms of elementary bodies, as drawn in the Text-Figure, are recognizable. An arrangement in pairs of the elementary bodies is seen, as indicated by brackets.

N, nucleus of the epithelial cell; *P*, suspicious "polygon." Figure 9, × 12,800; Figure 10, × 22,000.

space between the cavity wall and the colony of inclusion bodies. This space is probably due to an artificial detachment. Nevertheless, easy formation of such a detachment may suggest that the cellular elements and the inclusion bodies are heterogeneous substances with respect to each other.

In most typical inclusions the inclusion bodies consist of distinct granules. When examined at a high magnification, the granules are round or elliptic in shape (Figs. 8, 9, and 10). The structure of the granules is not uniform. As indicated by the Text-Figure, the following forms are found: (1) spherical membrane with low-density content; (2) membrane with low-density cortex and moderately dense, not sharply defined central body; (3) membrane with low-density cortex and very dense, distinctly defined nucleoid; (4) very dense granule with moderately dense surrounding cortex; (5) very dense granule without surrounding structure, and (6) variations of these forms.

The membrane is generally thin. It may often be incomplete, and then it looks like a broken membrane. In some cases, however, the membrane may be thick.

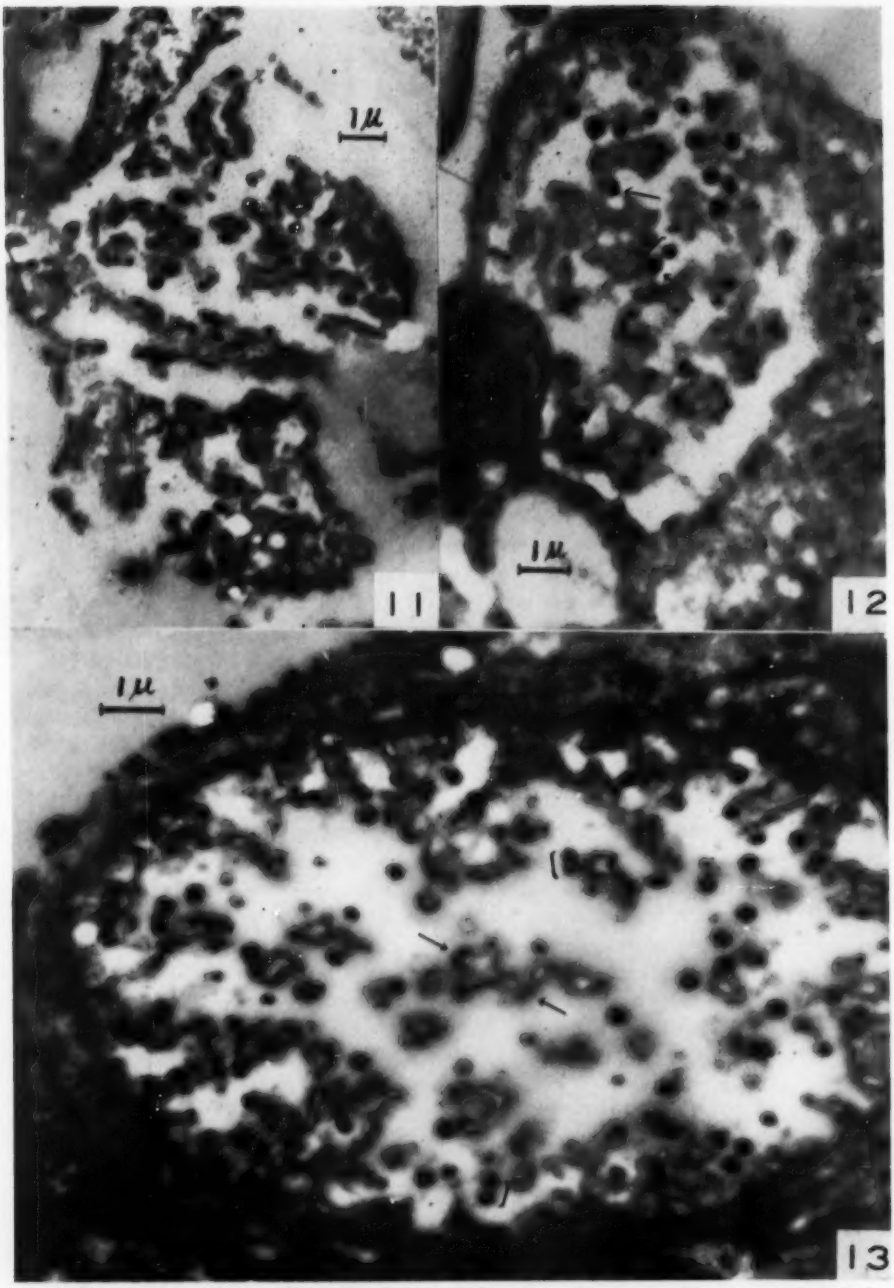
The dense granule and the nucleoid sometimes seem to have internal structures. A low-density zone is often recognizable between the wall and the center of the granule, and then the granule looks like a thick wall with central spot. The granules are very often arranged in pairs, suggesting multiplication by binary fission (Figs. 9 and 10).

The size of the membrane sphere is usually in the range of 400-500 mμ. The size of the nucleoid and the solid granule is in the range of 200-350 mμ. There are, however, some exceptionally large solid granules, which measure over 400 mμ. The maximum limits of the size range given above may indicate the accurate figure, while the minimum limits may involve some uncertainties, because a lateral section of an element may make it appear of smaller size than it actually is.

The morphology of the inclusion bodies mentioned above has many similarities with that of pox viruses, as reported by Gaylord[4] and others. There may remain no doubt that the epithelial inclusion body in trachoma is the colony of the actual trachoma virus.

The inclusion findings mentioned above are the most representative and predominant in the chronic case. No doubt, the findings correspond to those of the "elementary-body inclusions" with a light microscope. As described in the previous section, with a light microscope, most "elementary-body inclusions" are seen actually to consist of a mixture of a large number of elementary bodies with a small number of initial bodies. The elementary bodies measure about 250 mμ and most initial bodies about 500 mμ, although the size of the latter varies over a relatively wide range.

The problem then arises as to what findings with the electron microscope would correspond to the elementary and initial body respectively, seen with the light microscope. The sphere membrane with the electron microscope measures 400-500 mμ. However, as seen in Figures 9 and 10, the sphere membrane with nucleoid is a predominant component of the inclusions of this type. It seems reasonable, therefore, to consider that the nucleoid is stained by the Giemsa method, while the membrane and low-density cortex are hardly stained. Thus, the nucleoid (and the solid granule) appear as elementary bodies with the light microscope. Some exceptionally large solid



Figs. 11, 12, and 13.—Elementary-body inclusions in earlier stages. The corpuscular viral elements are four in number. On the other hand, an amorphous substance, which shows a polygonal structure in Figures 12 and 13, is pronounced (polygons). Some of the granules appear to be formed by a condensation of the polygons, as indicated by arrows. An arrangement in pairs of the solid bodies is also recognizable, as indicated by brackets. Figures 11 and 12, × 500; Figure 13, × 9300.

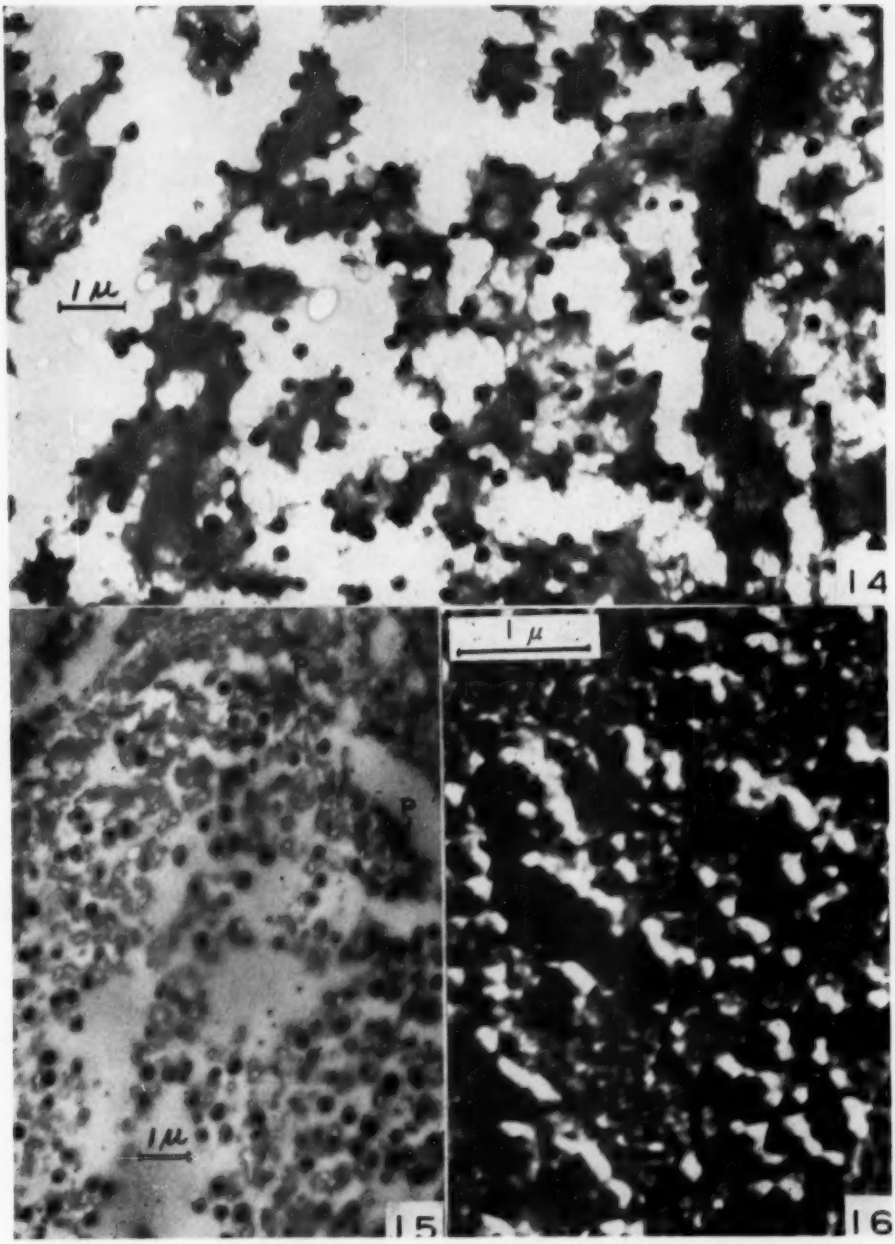


Fig. 14.—Granules apparently being formed by a condensation of the processes of a polygonal mother substance. × 10,000.

Fig. 15.—Small polygons, which may be related to huge polygons, are obvious. *P*, suspicious huge polygons. × 7500.

Fig. 16.—Elementary bodies in a purified material. Formation of a conglomeration is obvious. Chrome shadowing; × 20,000.

granules, which measure over 400 mμ, as seen in Figures 7 and 8, may correspond to the initial bodies that are found in the "elementary-body inclusions" by the light microscope.

2. *Earlier-Stage Inclusions.*—Inclusion bodies in smaller cavities have a feature slightly different from that of typical elementary-body inclusions. The former may probably be in an earlier stage than the latter. The inclusions indicated by IB_1, IB_2, and IB_3 in Figure 5 represent such earlier inclusions. In this case, the nucleus of the cell has not yet been pushed to one side, although it sometimes shows a wane, as IB_1. Figures 11 and 12 show representative inclusions at a higher manification. Figure 7*P* and Figures 13 through 15 seem to show inclusions of this kind at a little more advanced stage.

The most characteristic feature of these inclusions is that the distinct granules are few in number and the amorphous substance is predominant. The amorphous substance very often shows a polygonal structure. The solid granules are sometimes incompletely spherical and are placed at a corner of the polygonal substance. The granules then look like a semispherical nucleus of a comet, having the amorphous substance as the tail, as indicated by arrows in Figures 12 and 13. They then give an impression that the solid granules are developed by a condensation of the amorphous substance.

3. *Earliest-Stage (Initial-body) Inclusions.*—The pure initial-body inclusions are not always easy to identify with the electron microscope. In the earliest stage of inclusion formation, it seems likely that the inclusion cavity is indistinct.

In Figures 17 through 22 the findings in all probability correspond to the initial-body inclusions seen with a light microscope, though not all of them are the pure form.

The inclusion shown in Figure 19 is situated by the nucleus in a cap form. Larger granules measure up to 800 mμ, and smaller ones, as low as 400 mμ. The smaller ones have a structure similar to that of initial bodies found in the "elementary-body inclusions." The larger granules have a different structure. There are, however, gradual transitions between the two. Figures 18 and 21 also seem to show pure initial-body inclusions; the former is a distinct cavity and the latter is not. In the former a huge polygonal finding is involved.

The finding shown in Figure 20 is most interesting. At the left side there is a group of typical elementary bodies. At the right there are large granules which are thought to be initial bodies. Figure 17 is a mixed inclusion of initial bodies and elementary bodies, in which the initial bodies are found in a relatively great number.

With a light microscope, pure and small initial-body inclusions very often show a rosette arrangement, and this fact may also assist in the identification of initial bodies by the electron microscope. Figure 22 shows a typical rosette arrangement of an initial-body inclusion. In this picture, a binary fission of initial bodies seems to be suggested by a fissure formation in some of the initial bodies. A rosette formation of initial bodies is also observable in Figures 18, 19, and 21.

It seems likely that the size of initial bodies varies greatly, in the range

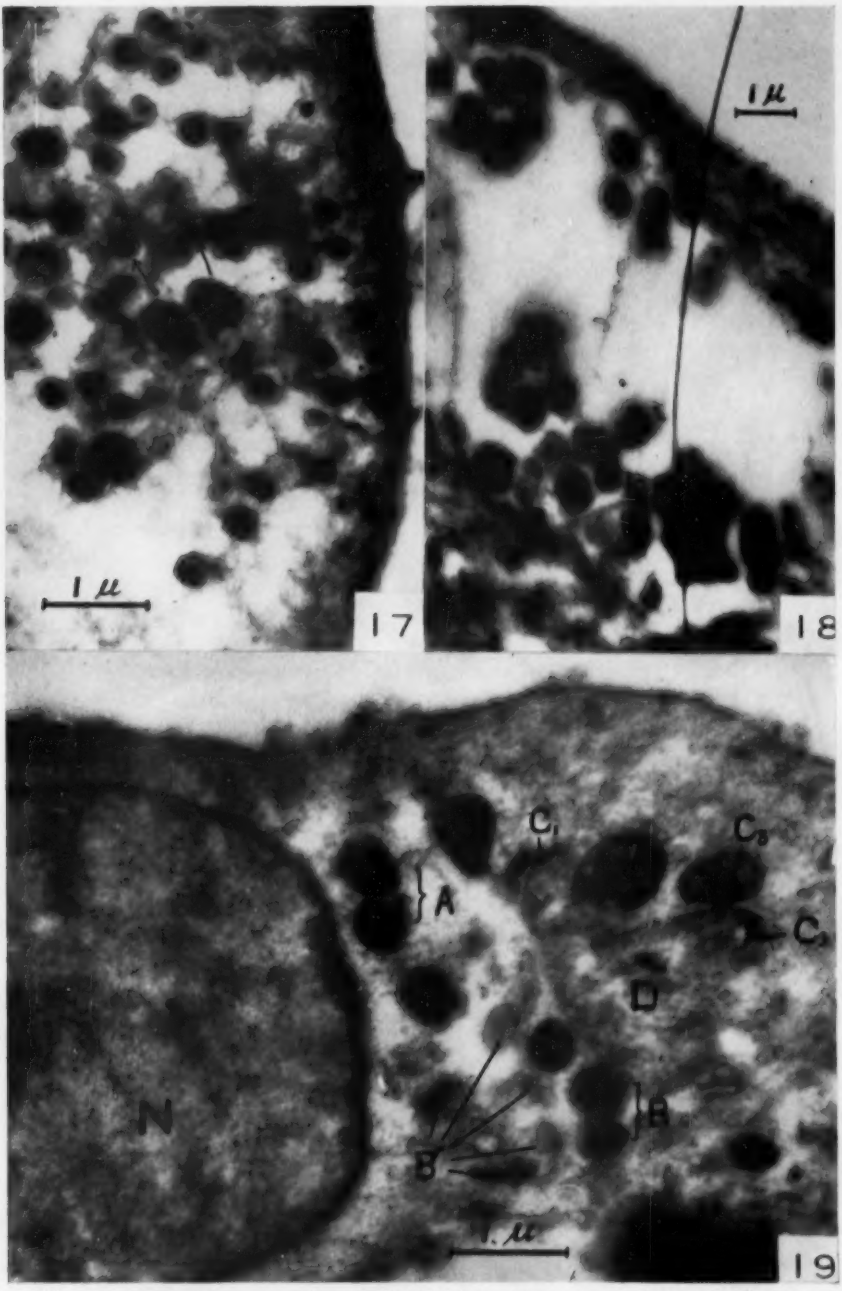


Fig. 17.—Relatively large number of initial bodies with elementary bodies. Hemispherical elementary bodies with amorphous tail are indicated by arrows. × 16,000.

Fig. 18.—A pure initial-body inclusion with a distinct huge polygon. × 9000.

Fig. 19.—A pure initial-body inclusion without distinct cavity. Initial bodies measure 400-800 mμ and are arranged in a rosette form. Some of them appear in pairs (*A,B*). There are some hemispherical bodies with amorphous tail (C_1, C_2), and they seem to be developing from a Y-shaped, huge "polygon" (*D*) by a condensation of its processes. C_3 and the largest body next to it may be initial bodies already fully developed from the same polygon. A number of still indistinct initial bodies appear to be developing in a rosette form in the other part of the cytoplasm (*B'*). *N*, nucleus. × 18,000.

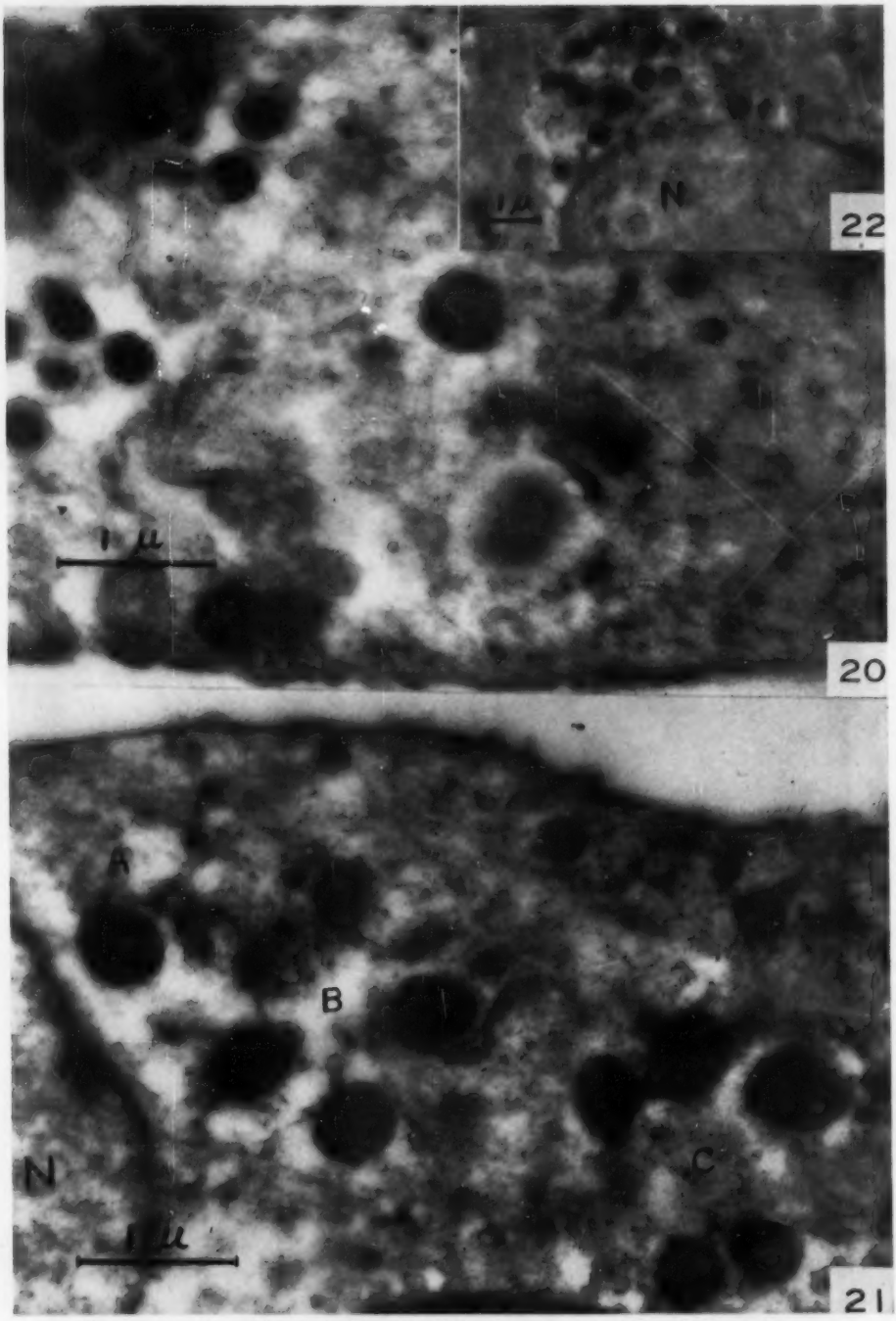


Fig. 20.—A colony of typical elementary bodies is seen at the left and top. A few grown-up initial bodies are seen in the middle and lower parts. More initial bodies seem to be developing. × 25,000.

Fig. 21.—A pure initial-body inclusion without distinct cavity. *A*, an initial body with multiple dense granules inside; *B* and *C*, initial-body rosettes. Three of the initial bodies in the rosette *B* are not sharply defined, and they are probably still developing. *N*, nucleus. × 25,000.

Fig. 22.—A cup-formed inclusion of initial bodies by the nucleus. A rosette formation is obvious. *N*, nucleus. × 8000.

of 400 to 800 mμ. The larger ones very often are oval, while smaller ones are apt to be round.

The larger initial bodies have various internal structures. Sometimes they show a reticular or an alveolar internal structure. Sometimes they contain a number of distinct granules. The smaller initial bodies are apt to have one solid granule inside.

There are gradual transitions from large initial bodies to small initial bodies and from the latter to typical elementary bodies. There seems to be no sharp line between the initial and the elementary bodies, regarding either the size or the structure.

4. *Life Cycle of Trachoma Virus.*—It has been believed that trachoma virus has a definite life cycle. It is believed that when an elementary body enters into a host cell it begins to grow to form an initial body. By repeated binary fission of the initial body, there finally develops a colony of elementary bodies.

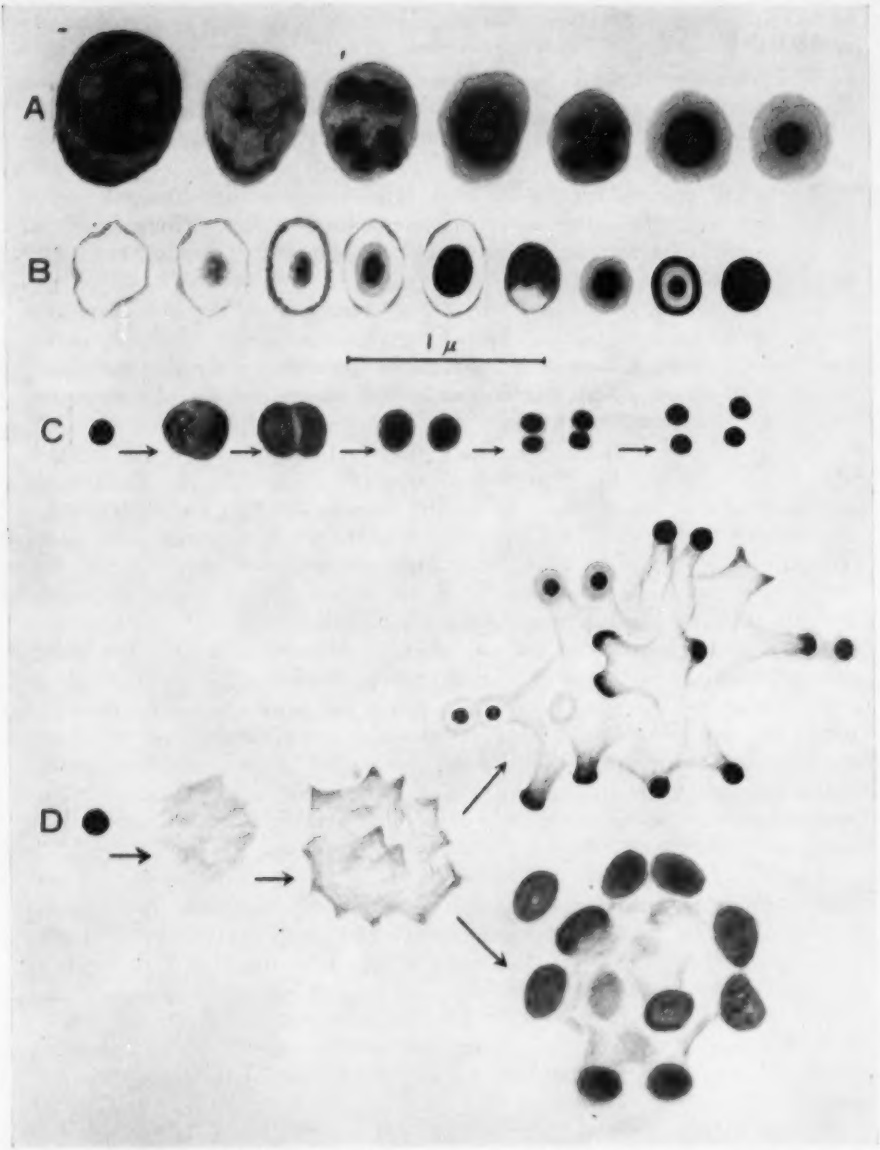
The following findings concerning the trachoma virus by the electron microscope may not be contradictory to this conception: (1) Initial-body inclusions are by far the most frequently demonstrated in the earliest stage of trachoma infection; (2) a binary fission of the trachoma virus is suspected from a fissure formation (Fig. 22), dumbbell-shaped elongation (Fig. 18), and Diplococcus-like arrangement (Fig. 19 *A* and *B*) of initial bodies, as well as the very often recognizable arrangement in pairs of elementary bodies, as already described, and (3) gradual transition of large initial bodies to small ones and further to the elementary bodies.

However, by electron microscopy, there are still some other findings which are hardly explained by the conception mentioned above. They are the presence of amorphous substance which very often shows a polygonal structure, and the hemispherical viral granules with amorphous tail. This feature has been described in the section on the earlier-stage inclusions. The same thing can also be seen in the initial-body inclusions.

The initial bodies indicated by C_1 and C_2 in Figure 19 show a typical hemisphere with amorphous tail. There seems to be a Y-shaped polygonal substance joining these initial bodies (*D*) and several other initial bodies seem to be developing in it. The C_2 and C_3 are arranged as a pair. However, they do not seem to have been developed by a binary fission of one body. It seems rather likely that C_3 is a fully developed initial body and that C_2 is a successfully developing one from the same polygonal mother substance. There seems to be developing rosette by a condensation of the amorphous substance (*B*).

In the finding indicated by *C* in Figure 21 there appear to be two pairs of initial bodies. This finding may be interpreted to mean that the two pairs are produced by a hexagonal mother substance at the center as the processes of it. The polygon in Figure 18 suggests also such a developmental course of the trachoma virus.

There seems to be a possibility of the following developmental pattern of the trachoma virus, although we are not claiming this new conception. We are also not going to replace the previous conception with this new one. We are merely stating this new hypothetical conception, supposing a possibility of it (Text-Figure *D*).



Text-Figure.—*A*, *B*, schematic diagram of various forms of corpuscular elements of Chlamydozoon trachomatis found in trachomatous conjunctiva. *A* corresponds to initial bodies and *B* to elementary bodies in a light-microscopic finding. The scale, showing μ, is applicable to *A* and *B*.

C, *D*, two patterns of the developmental cycle of C. trachomatis. *C* shows the pattern accepted in general, based on light-microscope findings. In a new host cell, an elementary body develops into an initial body. By repeated binary fissions of the latter, a colony of new elementary bodies results. *D* shows a new hypothetical pattern suggested by electron-microscope findings. A "vegetative form" of the virus develops from an elementary body in a new host cell. The "vegetative form" is at first an amorphous substance. Then it is apt to show a polygonal structure. Corpuscular elements, initial and elementary bodies, are formed from the vegetative form by a condensation or like process.

When an elementary body enters a host cell, it dissolves into the host cell. Then production of a large amount of amorphous viral component results. The amorphous viral component then begins to condense, often showing a polygonal structure, to form new corpuscular viral elements by a condensation, or like process. In some conditions, probably in the cell with little immunity, it is apt to form larger granules, the initial bodies. In others, probably in cells with a relative immunity, it is apt to form smaller granules, namely, the elementary bodies.

The amorphous mother substance is, therefore, something like a "vegetative form" of trachoma virus. The elementary body may be a "spore." The initial body may be a transition form of the two. It may, further, produce elementary bodies by binary fission or by breaking into several elementary bodies.

5. *Some Unidentified Findings.*—Figures 23 through 26 are inclusion-like findings very often observed in the epithelium of the acute-case. The interpretation of these findings is still inconclusive. However, most, if not all, of them seem to be viral elements in various developmental stages.

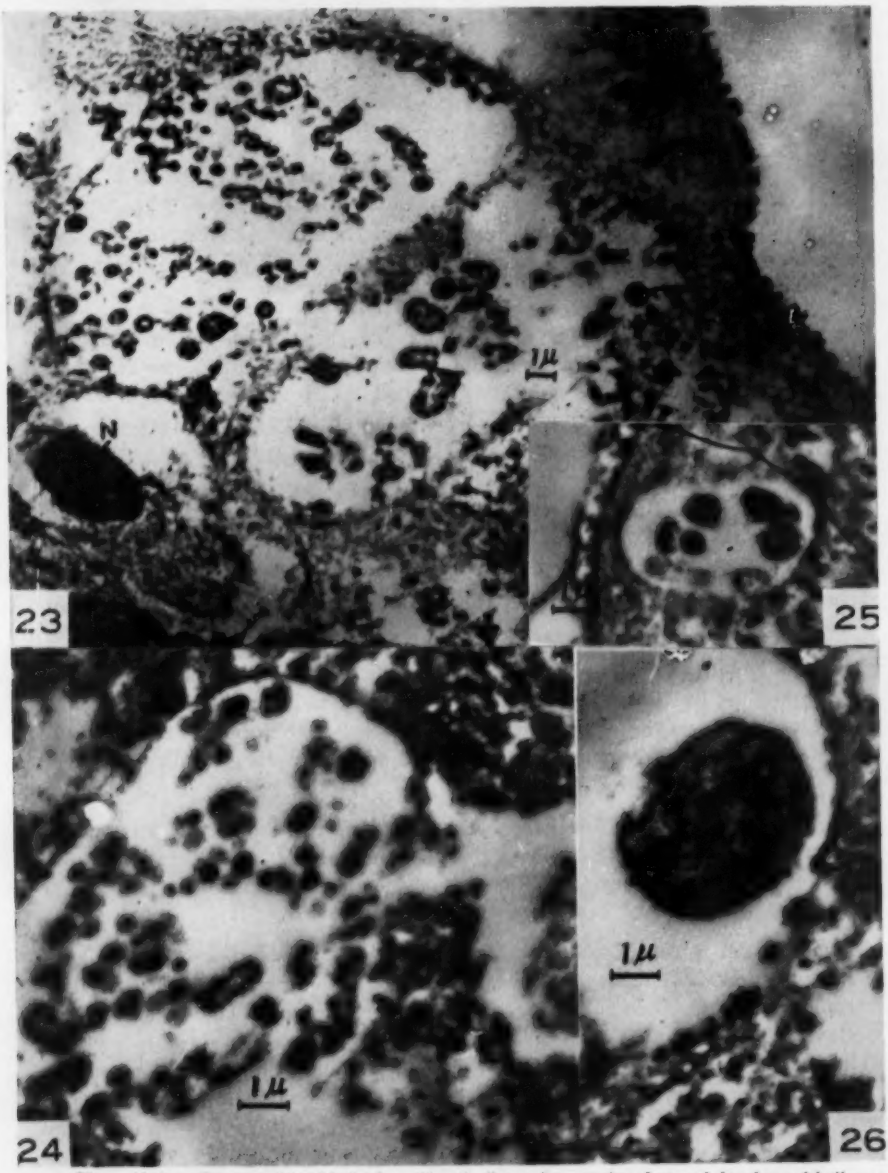
The structure indicated by *A* in Figure 27 is also one of the unidentified findings. The first thing suspected is a mucous cell. However, in case of a mucous cell, the secretion granules do not reach the nucleus (Fig. 28). A detachment of the alveoli from the cytoplasmic wall cannot be seen. It is rare to find a mucous cell in the epithelium with a nest of inclusions. It may, therefore, be possible that this alveolar finding is a huge "vegetative form" of the trachoma virus.

6. *Subepithelial Trachoma Virus.*—We looked for virus-like findings in the subepithelium as far as possible. So far, however, corpuscular, virus-like granules have never been found in the subepithelium. The granules found in the subepithelium were identified as leucocyte granules, mast-cell granules, or mitochondria.

7. *Conglomeration of Trachoma Virus.*—In the previous study, it was our experience that trachoma virus was readily purified by a differential centrifugation. The potent material was found in the sediment of a preliminary centrifugation, and not in the supernatant fluid.

During the present study, the trachoma virus was supposed to make a conglomeration. We thus employed a method of differential centrifugation recommended by Ozaki[5] in infectious ectromelia virus. The method is as follows: Trachomatous conjunctiva is sectioned by a freezing microtome. The sections are suspended in purified water for one night in a refrigerator. Then a preliminary centrifugation is done at 1000 rpm for one minute. The supernatant fluid is again centrifuged at 3000 rpm for 60 minutes. The sediment is suspended in purified water and is examined by the electron microscope after chrome shadowing. Figure 16 is a picture thus obtained. When the final supernatant fluid was centrifuged at 12,000 rpm for 30 minutes, the sediment contained almost no corpuscules.

It is not clear whether the granules in this picture are actual elementary bodies or not. If they are, however, they appear to make conglomerations.



Figs. 23-26.—Some unidentified virus-like findings frequently observed in the epithelium of the acute case. If not all, most of them are supposed to be developmental stages of C. trachomatis. Figure 23, × 4500; Figures 24-26, × 7500.

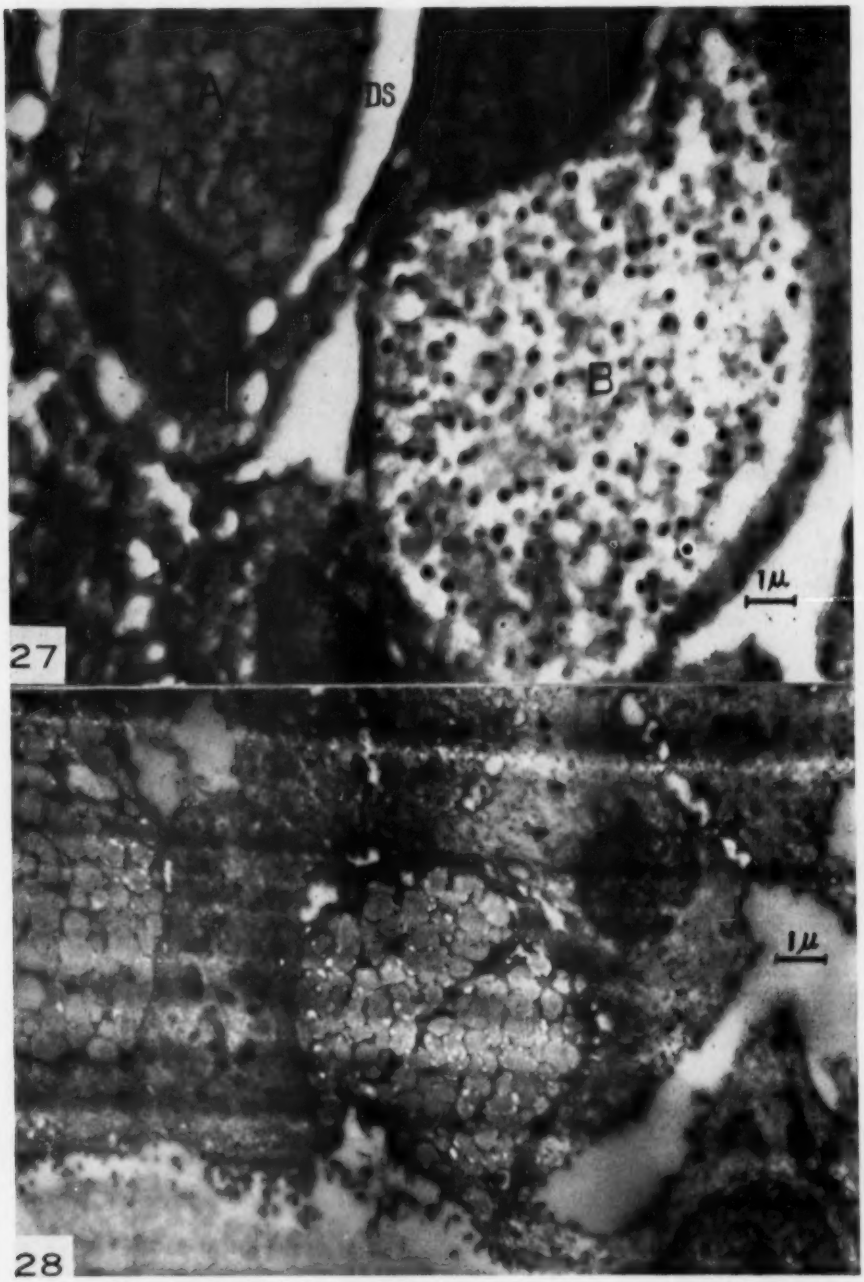


Fig. 27.—*A*, unidentified finding. This is probably a huge "vegetative form" of C. trachomatis. A polygonal structure, as seen in Figure 12, is recognizable, and some elementary-body-like granules are seen inside, as indicated by arrows. Many other granules appear to be developing throughout the mass. The mass reaches the nucleus, and there is a detached space between the mass and the cytoplasmic wall (*DS*).

B; typical elementary-body inclusion. *B* looks like a next stage of *A*. × 7500.

Fig. 28.—Mucous cells. The secretion granules do not reach the nucleus. There is no detached space between the mass of the secretion granules and the cytoplasmic wall. × 7500.

Summary and Conclusions

This investigation is a study of trachoma virus by the electron microscope in thin sections.

Intracellular corpuscular viral elements are found in the epithelial cells exclusively. They are usually found in a cavity of the cytoplasm of epithelial cells except in case of the earliest initial-body inclusions.

The elementary bodies and initial bodies, as observed by a light microscope, are also distinguishable by the electron microscope. However, there is not a sharp line between the two. There are transition forms.

The elementary bodies are usually round or elliptic in shape and measure 200 to 300 mμ, when an inconstant external membrane is neglected. The diameter of the inconstant external membrane sphere is about 500 mμ. The initial bodies are round or oval in shape and measure up to 800 mμ.

An amorphous substance, which often shows a polygonal structure, is frequently found in connection with the viral corpuscules. There are findings which suggest that the corpuscular elements are produced by a condensation of the polygonal mother substance. We consider the possibility of the presence of a hypothetical "vegetative form" in the life cycle of trachoma virus, although we do not deny a development of elementary bodies by a binary fission of initial bodies.

We were not able to find any virus-like structure in the subepithelial tissues of trachomatous conjunctiva.

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Eyelid Coloboma with Cutaneocorneal Bridge

Capt. ROY R. SINGER (MC), U.S.A.F.

Congenital coloboma involving the inner third of the upper eyelid is not an uncommon anomaly, particularly if it occurs unilaterally. Less often, however, is the defect noted to contain a bridge of skin intimately adherent to the sclera and cornea of the underlying globe, with absence of the upper canaliculus and apparent lack of a caruncle on the affected side.*

Pathogenesis of so complex a defect is logically attributed to the occurence of an amniotic band (whose remnant is the cutaneocorneal bridge), strangulating mechanically the development of structures normally present in the colobomatous area. This explanation seems not inconsistent with the opinion of Seefelder † that localized failure of adhesion of the lid folds, normally complete in the 35 mm. embryo, results in localized absence of lid margin structures. Of necessity, the amniotic band must be operative prior to the 35 mm. stage.

In a case of bilateral congenital coloboma of the upper eyelid occuring in a mentally retarded 4-year-old Mexican boy, Potter [2] noted the existence of clouding of the nasal half of the right cornea, from the central area of which a band of vascularized conjunctiva extended upward and nasally. The left globe was free of any change, despite the presence of a symmetrical lid defect. His findings, in conjunction with the accepted theory of pathogenesis and the following case report, suggest that the amniotic band may undergo a wide variation in degree of development, i.e., from appearing indistinguishable from contiguous skin to complete absence at birth.

Report of Case

A 9-day-old Filipino boy entered the 6208th U.S.A.F. Hospital on February 28, 1956, because of the unusual appearance of his right superior palpebrum, which was believed by the referring physician to represent an anomalously developed eyelid.

The father was 28 years of age, free of congenital ocular defect, and his parents as well as his seven siblings were reported to be similarly without involvement. The child's mother, age 26, had five siblings and parents free of known ocular defect. This pregnancy was her first, terminating without incident in the delivery of the 6 lb. 5 oz. infant.

Physical examination revealed no evidence of abnormality, with the exception of mild cephalhematoma (left parietal) and a coloboma of the right superior palpebrum. The defect was roughly quadrilateral in configuration, with the medial

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* References 1 and 3.

† Cited by Duke-Elder.[1]

third of the upper lid being supplanted by a loose band of soft skin adherent to the superior nasal quadrant of the globe, extending onto the superior nasal quadrant of the cornea for a distance of 2 mm. The right lacrimal caruncle appeared absent. Superiorly, the band of skin was continuous with the skin of the brow, indistinguishable from it. The cornea surrounding the area of attachment was clear, as was the anterior chamber, and the conjunctiva in all other areas was free of anatomic abnormality.

Fig. 1.—Appearance with the colobomatous eyelid closed.

Fig. 2.—Eye open, with the cutaneocorneal bridge evident nasally.

Only a small area of cornea was exposed upon ordinary closure of the right eye. Ophthalmoscopy under mydriasis revealed no additional abnormalities of the media or fundus, bilaterally. (The left eye was normal in all respects.)

Surgical reconstruction of the upper lid, with removal of the cutaneocorneal bridge and repair of the conjunctival defect, is contemplated.

Summary

A case of unilateral coloboma of the eyelid with cutaneocorneal bridge is reported. Theories of pathogenesis are adduced, along with a suggestion of the significance of the highly differentiated cutaneocorneal bridge present.

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Reading Glasses for Patients with Very Poor Vision

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and
ROBERT M. STURMAN, M.D., New York

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(3) Restriction of the "Field" by an Eyeglass and by a Loupe
(4) Magnification by a Telescopic System

Introduction

Psychologically, a literate person need not be considered "blind" as long as he retains the ability to read ordinary print. If he is still able to read a newspaper, a book, or a typewritten letter, he belongs to the community of seeing men.' Patients whose vision is less than 20/200 and are unable to carry on with the usual reading glasses may learn Braille's reading system, but they are excluded from the life of normal, seeing human beings.

Some patients with poor vision succeed in finding a magnifying lens or some other optical device with which they are able to read, but they do so only by trial and error.

This paper will deal with the following questions:

What kinds of reading devices are available?

Is there a fixed relation between the visual acuity found with Snellen's chart and the ability to read at a close distance?

If such a relation exists, is it possible to find the required reading device by an exact computation based on distance vision?

To what degree of poor vision may a device still enable the patient to read ordinary print?

Which devices must be used in various degrees of poor vision?

A. Kinds of Reading Devices for Patients with Poor Vision (Amblyopia*)

Practically, there are three kinds of devices:

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From lectures by Dr. Kestenbaum on "Reading Glasses for Patients with Poor Vision" before the American Academy of Ophthalmology and Otolaryngology, New York, Sept. 22 and 23, 1954, and Chicago, Oct. 10 and 11, 1955.

* The term "amblyopia" is used in this paper for "poor vision" after correction of refractive errors, regardless of the cause of the poor vision.

1. A "magnifying eyeglass," that is, a strong plus glass used as an eyeglass, allowing the letters to be brought closer to the eye
2. A "magnifying lens," or "loupe"
3. A telescopic loupe

Other complex reading devices, such as projection of the letters upon a screen, are not dealt with here because they are not available for the daily life.

B. Magnifying Eyeglasses

In small degrees of amblyopia down to a vision, let us say, of 20/50, and with insufficient accommodation, we were used to "adding" a stronger plus glass to the "distance glass" than we did for persons with normal vision, employing the method of trial and error.

Can the required strength of the "added" plus glass be computed from the "visual acuity" of the patient, as found with Snellen's chart?

I. Near Vision *vs.* Far Vision

Such a computation would presume that the visual acuity found with Snellen's chart at 20 ft. ("far vision") and the visual acuity found with Jaeger's chart or some other reading chart at reading distance ("near vision") are identical, or at least comparable.

Snellen's chart is based on the assumption that a visual angle of one minute corresponds with the minimum separable for the "standard" eye, each letter subtending an angle of 5 minutes. Vision of 20/20 means that the eye can read at 20 ft. letters that subtend a visual angle of 5 minutes at a distance of 20 ft. As a matter of fact, the vision of a normal eye is usually better than 20/20, its minimum separable being less than one minute; but, conventionally, 20/20 has been accepted as the "standard" vision.

Jaeger's reading charts are based on the same principle. Jaeger 1 can be read at 36 cm. by a "standard" eye (20/20) if the accommodation is adequate; at 36 cm, distance, a letter of Jaegar 1 subtends a visual angle of 5 minutes.

On older Jaeger charts, the maximum distances at which a "standard" eye (20/20) with an adequate accommodation or with an "added" plus glass can read the various test lines are noted as follows:

Distance, Cm.	Jaeger Type
36	1
50	2
70	3
90	4
102	5

The "near vision" of an eye, i.e., its visual acuity for close distances, can be tested by measuring the farthest point at which, e.g., Jaeger 1 can still be read, of course with adequate accommodation or correction.

If, for example, an eye, in spite of adequate correction, cannot read Jaeger 1 at more than 18 cm. (instead of the "standard distance" of 36 cm.), the near vision of this eye is only one-half of the near vision of a standard eye. In other words, the minimum separable for this eye is twice as large as for the standard eye. A limit of 9 cm. for Jaeger 1 means one-fourth of the "standard near vision," etc. Similarly, Jaeger 3, with a standard distance of 70 cm., or Jaeger 5, with a standard distance of 102 cm., can be used as a criterion for the measurement of the "near vision" of an eye.

Recently, other kinds of reading charts have been used instead of the

original Jaeger charts. Some of these charts note the distances at which the text lines can be read by the "standard" eye, such as 0.50 meter, 0.75 meter, etc. The calculation of these distances is based on a principle similar to that of Jaeger's charts (an angle of 5 minutes for the letter); an eye that can read the "0.50" line at only 25 cm. has a "near vision" of one-half the "standard."

Since Snellen's chart and the reading charts are based on the same principle, "far vision" and "near vision" of an eye should, a priori, be equal.

Numerous observations by us have shown that there is actually a close correspondence between "far vision" and "near vision," except for five conditions, three of which may be explained by the constriction of the pupil in near gaze.

"Near vision" may be better than "far vision" in eyes with peripheral corneal opacities or with peripheral lens opacities, since a peripheral opacity is less disturbing if the pupil is narrowed.

2. Near vision is poorer than far vision in eyes with central opacities of the cornea and in eyes with central opacities of the lens, since the normal peripheral parts are covered by the iris in miosis. The favorable effect of a mydriatic on the reading ability in cases of nuclear sclerosis of the lens is known.

CASE 1.—Age 60, with nuclear sclerosis of the left lens. Vision: O.D. 20/20; O.S.—7.00 D.=20/100. Without the glass, the left eye read Jaeger 9 (normally visible at 172 cm.) only at 15 cm. After dilatation of the pupil, the left eye read Jaeger 2 at 14 cm. Here the nuclear sclerosis decreased the near vision to one-fourth normal if the pupil was dilated, to one-fifth normal for far gaze (with correction), and to one-eleventh if the pupil was constricted in near gaze.

CASE 2.—Age 49. O.D. posterior cortical cataract "in oculo coeruleo"; O.D.+3.50 D. cyl, ax 20=20/40; with added + 1.50 D., the eye read Jaeger 6 at approximately the usual reading distance. After dilatation of the pupil, the right eye with added +2.00 D. could read Jaeger 1 at 32 cm.

3. Near vision may be better than far vision in eyes with an incorrigible (e.g., irregular) astigmatism. As a simple calculation shows, the radius of the circle of diffusion decreases in proportion to the radius of the pupil.

The favorable effect of a pinhole disk on the far vision in astigmatism is illustrative.

4. Near vision, measured with the reading chart, is often poorer than far vision, measured with Snellen's chart, in cases of incomplete central scotoma or of field defects that reach the center (Cases 6, 7, 8, and 12).

This observation might be explained as follows: In a lesion of the macula itself, as well as in a lesion of the papillomacular bundle, not all points of the macular region may be damaged to the very same degree; some points may function more poorly than those between. The macular area may be compared to a kind of sieve.

In tests for far vision with Snellen's chart, the patient merely has to recognize isolated letters; on the other hand, the "near test," with a reading chart, requires reading, not spelling only. Even if the patient recognizes single letters, the presence of the "holes" may make reading, the integration of the letters into words, impossible.

This explanation is sustained by the observation that such an eye may not be able to "read" a larger text of Jaeger's chart but is able to recognize single letters of even a smaller text. In some of these cases practice may result in improvement of reading (Cases 6, 13, and 17).

5. Near vision may be better than far vision in pendular fixation nystagmus,

in which the nystagmus decreases, or even disappears, with convergence upon a near object.

CASE 3.—Age 11. Myopia; pendular fixation nystagmus. If one eye is closed, the nystagmus becomes jerky to the side of the open eye. The nystagmus stops almost entirely with convergence upon an object at a distance of 20 cm. O.D.—9.00 D.=20/120; O.S.—9.00 D.=20/100; O.U. 20/80. The poor uniocular vision is obviously due to the "superimposed latent nystagmus." However, the patient reads Jaeger 1 at about 15 cm. (instead of the normal 36 cm.). The relatively good near vision may be explained by the disappearance of the nystagmus in convergence.

In summary, near vision is better than far vision in incorrigible astigmatism, in peripheral opacities of the cornea or of the lens, and in some cases of nystagmus; near vision is poorer than far vision in central opacities of the cornea or of the lens and in case of an incomplete central scotoma.

An additional source of an apparent disproportion between "near vision" and "far vision" is given in the fact that the far vision found with a projected chart does not always equal the far vision found with a printed Snellen chart. In retinopathy, the printed chart sometimes indicates a better far vision than does the projected chart. In such cases the near vision, tested with printed texts, was found to conform with the far vision found with the printed chart.

When the enumerated conditions were taken into consideration, far vision and near vision were almost invariably found to correspond with each other. Therefore, the basis for computation of the required reading glass from the "far vision" as determined with Snellen's chart may be regarded as established.

In Conditions 1, 3, and 5, the near vision is even better than the far vision; the near glass, computed from the far vision, will surely enable the eye to read the intended text. In Condition 2, the use of a mydriatic (eucatropine [Euphthalmine] or phenylephrine [Neo-Synephrine]) may be recommended for reading. Only in Condition 4, i.e., in a partial central scotoma, the reading glass, computed from the far vision, may be too weak, and a stronger glass (50% and more) than resulted from the computation must be prescribed.

II. Computation of the Required Reading Glass from the "Far Vision" Found

(*a*) *Reciprocal of Vision* (RV).—The computation may be facilitated by introducing the concept of the "reciprocal of vision." With a given vision of 20/40 (=½), the reciprocal of vision is 2; with 20/20, 20/100, and 20/200 the reciprocals of vision are 1, 5, and 10, respectively. In short, the sign RV may stand for "reciprocal of vision."

For eyes with very poor vision, the visual acuity is usually given in terms of finger counting (F.C.) at so-and-so many feet. Since a "standard eye" is able to count spread fingers, of average size, at approximately a distance of 200 ft., the "standard vision" is F.C. at 200 ft. F.C. at 1 ft. could also be expressed as 1/200; F.C. at 2, 4, and 10 ft., as 2/200, 4/200, and 10/200, respectively. In other words, F.C. can always be substituted by the denominator /200 in a fraction.

Hence, with vision of F.C. at 1, 4, and 10 ft., the reciprocals of vision, the RV's are 200, 50, and 20, respectively. In this way, the RV gives a simple, significant number for the degree of "amblyopia" in each individual case.

One may describe the RV in another way. The smaller the "minimum separable," the higher the visual acuity, and vice versa. The RV is a numerical description of the minimum separable for the examined eye, as compared with that of the "standard eye." An RV of 2, 3, or 6 means that the minimum separable for this eye is 2, 3, or 6 times as large as that for the "standard eye," that is, 2, 3, or 6 minutes, respectively.

(*b*) *Computation of Glass Required for Reading Jaeger 1.*—1. What glass has to be "added" for reading Jaeger 1 in a case with vision of 20/60 after correction? By 20/60 is meant that the eye can read only at 20 ft. letters that a standard eye could read at 60 ft. Therefore its visual acuity is one-third that of the standard eye; its RV=3.

Since the standard eye (vision 20/20) can read Jaeger 1 at 36 cm., an eye

with a third of 20/20 vision or an RV of 3, should read Jaeger 1 at one-third of 36 cm., or 12 cm. But in order sharply to see an object at 12 cm., a glass of +8.50 D., approximately, is required (if there is no available accommodation). Hence, an eye with an RV of 3 requires +8.50 D. for reading Jaeger 1, at 12 cm. distance.

This and the following computations are made with the assumption that no accommodation is available. Obviously, the available amount of accommodation has to be subtracted from the computed strength of the required added glass.

2. To obtain a general rule, an eye with a vision of $\frac{20}{20}$ may be assumed. Here the RV=n. This eye could read Jaeger 1 at $\frac{36}{n}$ cm. In order to see sharply at $\frac{36}{n}$ cm., a plus glass of $\frac{100}{\frac{36}{n}}$ =2.8 n D. is required. The number 2.8 is therefore the "factor" by which the RV of the examined eye has to be multiplied to give the "added" plus glass required for reading Jaeger 1.

This "characteristic factor" for a text of a certain size, e.g., 2.8 for Jaeger 1, is obviously the quotient of 100 divided by the maximal distance at which this text can be read by a "standard" eye; $\frac{100}{36}$ =2.8.

(*c*) *Computation for Other Reading Texts.*—1. Jaeger 3 can "normally" be read at 70 cm. distance. Its "characteristic factor" is therefore $\frac{100}{70}$ =1.4. The RV of the eye times 1.4 gives the plus glass required for reading Jaeger 3.

2. Jaeger 5 can "normally" be read at 102 cm. Its "characteristic factor is $\frac{100}{102}$, or, approximately, 1. The rule here is very simple. To read Jaeger 5, an eye requires as many plus diopters "added" as its RV, determined with Snellen's chart, amounts to.

In other words, if the vision is only $\frac{1}{n}$ of the normal vision, Jaeger 5 can be read only at $\frac{1}{n}$ of the normal "maximal reading distance" for Jaeger 5, i.e., of 1 meter; $\frac{1}{n}$ meter is the focal distance of the required glass. Hence a plus glass of diopters is required for reading Jaeger 5.

Examples: For eyes with 20/100 (RV=5), 20/200 (RV=10), and 20/400 (RV=20), +5.00, +10.00, and +20.00 D., respectively, have to be "added" for reading Jaeger 5.

3. In summary, the "characteristic factors" are as follows: 2.8 for Jaeger 1, 1.4 for Jaeger 3, and 1 for Jaeger 5.

4. If the "maximal reading distance" for each paragraph is noted in fractions of meters, 0.50, 0.75, and 1.50, the "characteristic factors" are the quotients of 100 (1 meter) divided by these numbers, i.e., 2, 4/3, and 2/3, respectively.

(*d*) *Tabulation of Common Reading Glasses.*—The figures that are of practical importance in amblyopia, down to a vision of 20/200, are presented in the accompanying Table. The required "added" glass is given in diopters; the reading distance,† in centimeters, with approximation. Reading distances of more than 40 cm. and glasses of over +15.00 D. are here omitted.

† The reading distances have to be measured from the eyeglass, not from the eye.

Reading Distances and Glass Strengths of Importance in Amblyopia

Vision (After Correction)	RV	For Jg 1, or 0.36		For Jg 3, or 0.70		For Jg 5, or 1	
		Lens, D. (Approx.)	Reading Distance, Cm.	Lens, D.	Reading Distance, Cm.	Lens, D.	Reading Distance, Cm.
20/200	10	.....	..	+14.00	7	+10.00	10
20/100	5	+14.00	7	+ 7.00	14	+ 5.00	20
20/80	4	+11.00	9	+ 5.50	18	+ 4.00	25
20/60	3	+ 8.50	12	+ 4.25	24	+ 3.00	33
20/50	2.5	+ 7.00	14	+ 3.50	28	+ 2.50	40
20/40	2	+ 5.50	18	+ 2.75	35	.....	..
20/30	1.5	+ 4.25	24	.....	..	.....	..

(*e*) *Accommodation and Reading Glass.*—Usually a portion of the required diopters is provided by the available accommodation. Only the remainder has to be "added" to the "distance" glass.

If the amount of available accommodation is not known, one determines the plus glass that brings the near point of the eye just to the "adequate" reading distance, as given in the accompanying Table.

Example: An eye with 20/100 vision after correction (RV=5) should be enabled by "added" +5 D. to read Jaeger 5 at 20 cm. Therefore, one determines the plus glass that brings the near point to 20 cm. Let us say, this glass is +2 D.; obviously, +3 D. has been provided by the accommodation. The +2 D. has to be "added."

(*f*) *Refraction and Reading Glass.*—The computed glass has to be "added" to the determined distance refraction of the eye. For example, an eye with −5 D. myopia and a vision of only 20/200 (RV=10) needs −5D.+10D.=+5 D. for reading Jaeger 5 at 10 cm. If this eye still has an accommodation of 5 D. or more, then it does not need a glass at all; it can read Jaeger 5 without any glass at 10 cm. distance.

In high myopia, the reading glass (distance glass+added RV diopters) may still be a minus glass (Cases 19 and 22).

(*g*) *Text Size to Be Selected* (Jaeger 1, Jaeger 3, or Jaeger 5).— With a fair approximation, Jaeger 1 corresponds with the small letters on stamps; Jaeger 3, with the letters in telephone books, and Jaeger 5, with the letters used in most of the newspapers and typewritten papers. The selection must be based on individual needs.

NOTE:—Most types of near work are done at approximately 30 cm., and reading Jaeger 3 is satisfactory for most occupations.

In certain professions, such as medicine, dentistry, and watch making, perception of details in the size of Jaeger 1 may be required. If such patients have poor vision, then, of course, they have to work at a very short distance. For example, a patient with 20/100 (RV-5) can read Jaeger 1 with +14 D. (5×2.8), but only at 7 cm. distance (from the eyeglass) and with one eye only.

Sometimes two pairs of near glasses or bifocals may be required, for instance, glasses "for Jaeger 3" at a greater distance (e.g., for reading musical notes) and another glass "for Jaeger 1" at a smaller distance.

The choice among magnifying eyeglass, magnifying lens (loupe), and telescopic loupe will be dealt with in Section D.

III. Microglasses and Related Glasses for Visual Acuity of Less Than 20/200

The use of a "magnifying eyeglass" of the usual size and kind has an upper limit. The spherical aberration caused by the peripheral parts of the eyeglass increases with the strength of the glass. In a "normal" eyeglass of +20 D. or more, the spherical aberration makes reading difficult (this limit applies to loupes, too).

(*a*) *Microglasses.*—This difficulty can be overcome by the use of a glass with a smaller diameter, formed like a lenticular glass. Since the peripheral parts are eliminated, the spherical aberration is diminished considerably. Most of the usual glasses have diameters of 35-45 mm. An eyeglass of +20 D. with a diameter of 30-32 mm. (a typical lenticular lens) still gives satisfactory sharpness. If the glass is stronger than +20 D., its diameter has to be still smaller. In this way, reading

glasses up to +50 D. and more have become available. Such small glasses have been called microglasses.‡

1. Computation of the Required Microglass: The computation of the required strong plus glass is similar to that described for weaker glasses. Since people with such poor vision are usually more than satisfied if they are enabled to read typewritten letters, i.e., approximately Jaeger 5, and since the "characteristic factor" of Jaeger 5 is 1, the required reading glass must have as many diopters as the RV of the eye amounts to.

An eye with 20/200 (RV=10) needs +10 D. to read Jaeger 5; eyes with finger counting (F. C.) at 10 ft. (=10/200), at 6 ft. (=6/200), and at 4 ft. (=4/200), or with RV's of 20, 33, and 50, need +20, +33, and +50 D., respectively, to read Jaeger 5.

2. Position of the Text in the Focal Point of the Eyeglass: As shown below, the magnifying eyeglass (microglass) may be regarded as a kind of magnifying lens (loupe) that is worn approximately 2 cm. in front of the nodal point of the eye, since the distance between eyeglass and cornea is usually 10-14 mm. and the distance between corneal surface and nodal point approximately 8 mm. Hence, according to Formula (8) (Appendix Sect. 1) its real magnification $M_r=\frac{D}{4}$ only if the object is at the focal point of the eyeglass.

If, for example, a glass of +20 D. is used, the object must be 5 cm. from the eyeglass—not from the eye—to give a magnification of $20/4=5\times$.

NOTE:—All "distances of the object" have, therefore, to be measured from the eyeglass, not from the eye.

Sometimes patients with poor vision, especially if they have not read for a long time, are not immediately able to read according to the theoretical calculation. It may be necessary at first to give a glass stronger than the calculation revealed (Case 23), have the patient practice, and then give the calculated glass, or to advise the patient at first to read only large print, such as the headlines of a newspaper, and then go over to normal print (Cases 4 and 5).

In any case, the calculated glass is the starting point of the examination for the required magnifying eyeglass. The patient must be instructed to hold the text exactly at the required distance (focal point of the glass). Since a deviation of even a few millimeters from the required (focal) distance may make reading impossible, the use of these glasses requires a certain amount of patience on the part of the physician and the patient.

3. Size of the Microglass: The following sizes for the microglass may be recommended: 30-32 mm. for +20 D.; 20 mm. for +33 D.; 15 mm. for +40 D.; 12 mm. for +50 D.

The smaller the eyeglass, the smaller is the number of letters that can be seen at once. According to a simple calculation (Appendix, Sect. 3), the number of visible letters is, approximately, 12 letters for +33 D. (20 mm.), 7½ letters for +40 D. (15 mm.), and almost 5 letters for +50 D. (12 mm.). See also Section D.

4. Advantages and Disadvantages of the Magnifying Eyeglass: The strong magnifying eyeglass (microglass) enables an eye with even exceedingly poor

‡ Kestenbaum, A.: Management in Amblyopia: Use of Microglasses, Conference of Eye Department, Mount Sinai Hospital, New York, March 5, 1942. Reference 1.

vision, down to "finger counting at 4 ft.," to read print of the size of Jaeger 5. Normally the vision of the perimacular area, up to a 10-degree distance from the center, is more than F. C. at 4 ft. Therefore, even an eye with an absolute central scotoma, occupying the entire macular area but sparing the perimacular area, an eye which is usually regarded as practically blind, may be able to read typewritten letters with a microglass (Cases 4-24).

If a strong microglass is used, the text has to be held very close to the eye; in using +20, +33, and +50 D., the text has to be held at 5, 3, and 2 cm., respectively, in front of the eyeglass. Since at such small distances even a few millimeters are crucial, the paper with the text must lie flat. Sometimes it is helpful to lay the paper upon a flat, rigid support, such as a cardboard.

It is very difficult therefore to find the proper strength of the glass and the proper reading distance by simple trial and error. The above calculation not only reveals the strength of the glass as required in the individual case but also gives the "distance" at which the patient must hold the text. This facilitates the instruction of the patient.

To read at such short distances as a few centimeters before the eyeglass is not very agreeable. While it would be prohibitive for a normal man, people who are practically blind will usually be happy if there is any possibility of reading at all. Such a strong glass allows monocular use only.

Obviously, there will be some people who regard reading as not so important for themselves, and nobody will compel them to do it. But there are numerous people for whom the ability to read will mean a new life.

5. Types of Magnifying Eyeglasses: (*a*) Microglasses. (1) Glasses up to +20 D., with a diameter of about 30 mm., are generally available (lenticular lenses).

(2) If more than +20 D. was required, at first microglasses were used in the form of linen testers or thread counters. These glasses are used commercially as a loupe for counting threads in material and are inexpensive.

The use of a linen tester as an eyeglass was the idea of a patient, F. Pollinger (in 1928). Because of bilateral central choroiditis, his vision was O. D.: F. C. 5-6 ft.; O.S.: F. C. 10 ft. He had attached a commercial linen tester of +50 D. by means of three wires to a spectacle frame. With this device he could read Jaeger 3 fluently. By holding another linen tester of +50 D. in front of the eyeglass, he had a glass of +100 D. With +100 D. he read Jaeger 1 fluently. This observation gave the initial impetus to the studies, which culminated in the formulas for the strength of the required glass.

The commercially produced linen testers or thread counters are of various strengths: +33 D., or "8 × magnification," +40 D., or "10 ×," and +50 D., or "12 ×."

For the relation between diopters and "magnification" see Section C.

Figure 1 shows various forms of linen testers. They consist of a small lens in a frame with a foot piece. The distance between foot piece and lens equals the focal distance of the lens.

Since the lens is sufficiently small, it gives a sharp image. Used as a loupe at the usual reading distance, a linen tester makes possible the counting of fine threads in fabrics, but not the reading of ordinary texts because it gives too small a field of vision. If, however, the lens is used as an eyeglass, the field is large enough for reading.

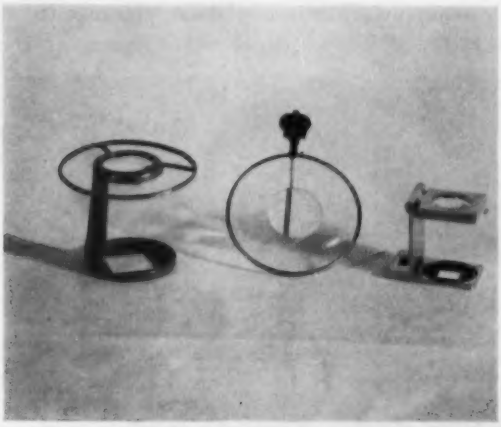

Fig. 1.—Various forms of linen testers.

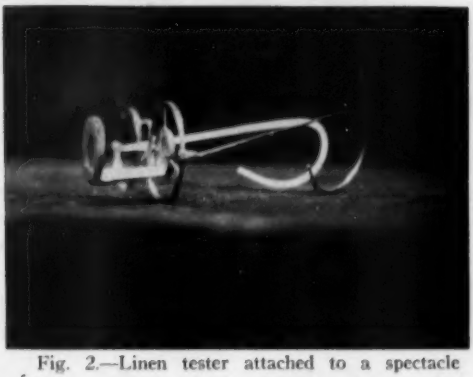

Fig. 2.—Linen tester attached to a spectacle frame.

A linen tester may be fastened to an ordinary spectacle frame (Fig. 2).

Since the foot piece of the linen tester lies at the focal plane of the lens, a paper pressed at the foot piece is at just the correct distance, namely, the focal distance of the lens. These primitive linen testers are now no longer used as final microglasses. But if a patient has a high degree of amblyopia and has not read for a long time, the use of a linen tester may still be advantageous. The patient presses the paper against the foot piece of the linen tester and thus learns to hold the paper at the exact distance. When he has learned to read in this way, he no longer needs a range finder and gets the final microglass.

(3) Later on, planoconvex lenses of the required strength and the required diameter were cemented upon a plane glass. These cemented microglasses are optically and cosmetically good and not expensive. They have only the disadvantage that they have to be cemented on again or renewed after one-half to one year.

(4) Recently, the American Optical Company has produced ground lenses according to suggestions of one of us (A.K.).

Figure 3 shows a set of test microglasses of various strengths and proper diameters. They may be put into a common trial frame: +16 D. (30 mm.), +20 D. (30 mm.), +24 D. (25 mm.), +32 D. (20 mm.), +40 D. (15 mm.), and +50 D.

(12 mm.). The glasses can be simply prescribed by stating the required strength and the adequate diameter of the eyeglass.

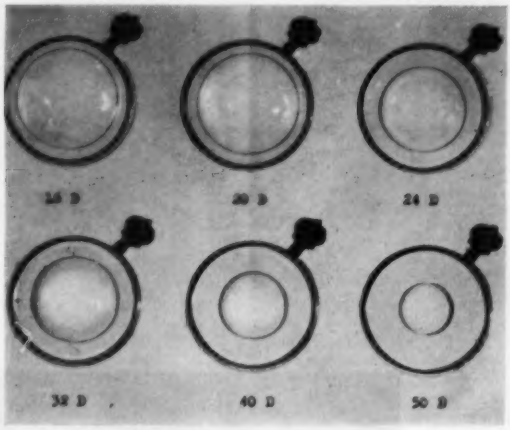

Fig. 3.—Ground microglasses.

Such a ground microglass is optically good and not conspicuous. The visual field is, of course, restricted by the circumference of the glass, but it is large enough for practical purposes.

(*b*) Other kinds of magnifying eyeglasses. In recent times the principle of magnifying eyeglasses as developed by Kestenbaum (1942, 1952) has been used in other methods, which also try to minimize the spherical aberration. In his so-called microscopic glasses, Feinbloom substitutes for a strong biconvex plus glass, let us say, a glass of +40 D., two planoconvex glasses of half the strength (+20 D.), the plane surface of the one lens standing in front of the convex surface of the other lens.

Linksz and Tait § used also two planoconvex glasses of half the strength, but with the convex surface of the one lens standing in front of the convex surface of the other lens.

Fonda ‖ uses small compound plus glasses, composed of several lenses, similar to Hartnack's loupes (Zeiss), fixed into a plane glass.

The first two forms are conspicuous, and the peripheral aberration is not very much diminished, but they have the advantage of a larger field. The third form, the compound lens, diminishes the spherical aberration, but the "field" is small and the lens is conspicuous.

It will depend on the individual case whether a less conspicuous lens or a slightly wider field is preferable.

Whatever form is chosen, a microglass or any other form, it is necessary to find the strength of the lens not by trial and error but on the basis of computation, as shown above. A patient with a vision of, let us say, 20/400 (RV=20) needs +20 D. or "5 × magnification" (see below) for reading of typewritten letters at 5 cm. distance; by trial and error, he may erroneously select, e. g.,

§ Linksz, A., and Tait, E. F.: Telescopic Lenses and Magnifying Systems, read before the American Academy of Ophthalmology and Otolaryngology, October, 1955.

‖ Fonda, G. E.: Subnormal Vision: Technique for Examination, read before the Academy of Ophthalmology and Otolaryngology, October, 1955. Reference 2. Kestenbaum, in discussion on Fonda.

+40 D., with which he reads at 2.5 cm. distance, or he may not find a glass at all.

The magnification by projection of the text by an apparatus upon a screen (up to 6 ×) can here be mentioned only briefly. The sharpness of the magnified text is here very good; the "field" is large. But this apparatus is too heavy to be carried around and can therefore be used only at one steady place. It is not available for the daily use.

C. Magnifying Lens (Loupe) and Telescopic Loupe

These reading devices will be discussed only briefly.

I. Magnification by a Loupe

The most important formulas for the magnification by a loupe are dealt with in the Appendix.

According to these formulas, a strong loupe gives the highest magnification if the object is in the focal plane of the loupe: "focal position of the object."¶

Loupes are usually labeled not according to their power, in diopters, but by their so-called "magnification," 2×, 3×, etc.

This "magnification" means the "real" magnifying effect of a lens. It equals one-quarter of its refractive power, measured in diopters, or $M_r = \frac{D}{4}$.

It must be stressed that this rule ($M_r = \frac{D}{4}$) refers to the "real magnification" and that it is valid only if the object lies in the focal plane of the lens and if the conventional 25 cm. is accepted as "standard" distance between object and eye. If, instead of 25 cm., let us say, 33.3 cm. were accepted as the "standard" distance between object and eye, the formula would be $M_r = \frac{D}{3}$.

This "real magnification" is, in contrast to the "angular magnification," independent of the distance between object and eye (Appendix, Sect. 1).

If the magnifying lens is fixed into a spectacle frame which is approximately at 2 cm. distance from the nodal point of the eye, the lens becomes a "magnifiying eyeglass." Therefore, the "magnification" of the "magnifying eyeglass" is also one-fourth of its power, in diopters, if the object lies in the focal plane of the glass.

II. Calculation of the Required Strength of the Loupe

The computation of the required strength of the loupe is like that of the strength of the magnifying eyeglass. A patient with 20/200 (RV=10) is able to read Jaeger 5 not only with an eyeglass of +10 D. but also with a loupe of +10 D. at any distance.

Since $M_r = \frac{D}{4}$, the computed number of required diopters need merely be divided by 4 in order to give the loupe required for the individual case.

Example: An eye with a vision of 20/100 (RV=5) needs a loupe of "5/4 magnification" for reading Jaeger 5; it needs a loupe of 5×1.4=7 D., or, approximately, of "2 × magnification," for reading Jaeger 3; it needs a loupe of 5×2.8=+14 D., or of "3½× magnification" for reading Jaeger 1 (if the object lies close to the focal point of the loupe).

¶ Often weak magnifying lenses are used, being held fairly close to the object: This may be called "subfocal" position of the object. The magnification is, of course, only low—less than two times. This means, e.g., that Jaeger 1 appears in the size of Jaeger 3, Jaeger 2 in the size of Jaeger 5, etc. These lenses are used by normal people for magnification of too small a text.

III. Restriction of the Field by Microglass and by Loupe

The edges of the lens limit the available field of vision or, if the eye is moved, the available field of gaze.

While a magnifying eyeglass and a loupe of the same strength offer the same real magnification, the size of the available "field" is different.

As shown in Figure 5, the available "field" is inversely proportional to the distance between lens and eye; a given lens used as a loupe, 20 cm. from the eye, allows one-tenth of the field obtained when used as an eyeglass at 2 cm.

Obviously, reading is more difficult when fewer letters can be visualized at once. Hence, the magnifying eyeglass has a great advantage over the loupe if a very strong lens must be used.

A simple calculation reveals the following (see Sect. B III): If the average size of a letter is assumed to be 2.5 mm., a 20 mm. large microglass of +33 D. allows the eye to see 12 letters at once, and a 12 mm. large microglass of +50 D., almost 5 letters; the same microglasses used as loupes, with the object at 20 cm., would allow only 1.2 and 0.5 letter, respectively. Such a tiny field still makes possible the counting of threads in material, but not the reading of words.

IV. Telescopic Loupe

The classical * telescopic system consists of a convex lens (objective) and a stronger concave lens (ocular), the two lenses being arranged at such a distance from each other that their second focal points coincide. In other words, the distance between the two lenses has to equal the difference between the "principal focal distances" of the two lenses.

Such a combination results in a twofold effect: On the one hand, light rays coming from infinity are made convergent by the convex lens and parallel again by the concave lens. On the other hand, the convex lens has a magnifying, the concave lens a minifying, effect.

The magnification of an object at infinity by a telescopic system is $-\frac{f_1}{f_2}$ if f_1 and f_2 are the focal distances of the two lenses, or $-\frac{D_2}{D_1}$ if D_1 and D_2 are the refractive powers of the two lenses.

If the object is at a nearer distance, these formulas are no longer valid. The closer the object, the less the magnifying effect of the system.

If a telescopic system is used as an eyeglass, in the form of so-called telescopic spectacles, it must not be too long. Since the magnification depends on the difference in strength between the two lenses, and since a greater difference requires a greater distance between the two lenses, the practical availability of telescopic spectacles is limited. The usual telescopic spectacles give a magnification of only 2.2 ×.

Addition of an adequate plus glass to the classical telescopic system changes it to a "telescopic loupe." A telescopic loupe, used as an eyeglass, makes possible magnification of letters at a more or less normal reading distance.

For the use of the telescopic loupe in practice, see below.

D. Practical Management in Various Degrees of Amblyopia

Amblyopia may be divided into three degrees.

See Appendix.

* Another kind of telescopic system consists of two convex glasses; the second focal point of the first lens coincides with the first focal point of the second lens. Such a system is not available for reading.

I. In slight degrees, down to 20/50 (RV=2.5), reading is possible by slightly increasing the "added" plus glass and bringing the letters slightly closer to the eye. The required "added" glass is found according to the formula: The required diopters equal the "reciprocal of vision," multiplied by the factor characteristic for the intended text size (2.8 for Jaeger 1, 1.4 for Jaeger 3, 1 for Jaeger 5). Available accommodation must be subtracted from the computed diopters.

Only in specific occupations, such as stamp collecting, may ability to see Jaeger 1 be required (D=2.8×RV). In most occupations one need read only "Jaeger 3," approximately corresponding with telephone book letters (D=1.4×RV), or even only "Jaeger 5," corresponding with approximately typewritten letters (D=RV).

Sometimes, the patient will prefer the slight magnification of a weak loupe held close to the object: "subfocal position of the object." Weak loupes (3-7 D.), held at a short distance from the object, magnify slightly, not more than twice.

II. In moderate degrees of amblyopia, let us say, from 20/60 (RV=3) to 20/200 (RV=10), one has the choice of three devices:

(*a*) The magnifying eyeglass, computed according to the above formula: D=RV (for Jaeger 5).

(*b*) The magnifying lens (loupe), computed according to the formula. The required "magnification" is $\frac{RV}{4}$ (for Jaeger 5).

(*c*) The telescopic loupe: The required "magnification" is also $\frac{RV}{4}$ (for Jaeger 5).

Each of the three devices has its advantages and disadvantages:

The magnfying eyeglass is inconspicuous, and neither hand is occupied with holding the device; but the reading text must be held close to the eye. In higher degrees of amblyopia, binocular vision is not possible, or only with an added strong prism.

The loupe allows the letters to be seen at a greater distance, but one hand must hold the loupe.

The telescopic loupe allows one to see the letters at a greater distance; neither hand is occupied by the device, but the telescopic loupe is very conspicuous and expensive.

The choice of the three devices depends on the individual requirements. If a great reading distance is required, a "loupe" or a telescopic loupe may be preferred; if this is not the case, the patient may prefer the less conspicuous magnifying eyeglass. Sometimes, the use of two devices is advisable, a magnifying lens or a telescopic loupe for reading at a fixed large distance, and a magnifying eyeglass for reading small texts (Case 21).

NOTE:—Whatever device is chosen, it should not be done by trial and error; the patient should never be sent to the optician to "find himself an adequate loupe." It should be prescribed on the basis of calculation.

III. In severe degrees of amblyopia, from 20/300 (RV=15) to F. C. at 4 ft. or 4/200 (RV=50), the telescopic loupe cannot be used, since sufficiently strong telescopic loupes are not available. A magnifying lens of the required strength provides so small a "field" that only a few letters can be seen at once. Therefore, practically, the magnifying eyeglass is the only available device for the daily life.† It may be in the form of the described microglass (ground, cemented, or made from a linen tester); if in a special case a wider field is necessary, one of the

† Magnifying projection by a stable apparatus (American Optical Company).

other, more conspicuous, forms may be chosen. But in any case the strength of the glass that has to be "added" in order to read typewritten letters must be based on the formula D=RV. The diameters of the microglass required for +20, +33, and +50 D. are 30, 20, and 12 mm., respectively.

If the eye is approximately emmetropic, the text has to be held just at the focal point of the reading glass. If the eye is severely ametropic, for instance, in aphakia, the text has to be held in the focal point of the "added" part of the glass (distance from the glass must be $\frac{100}{RV}$ cm.).

Example: Refraction is +10 D.; vision after correction is RV=15. The glass required for reading Jaeger 5 is +10+15=+25 D. The text has to be held in $\frac{100}{15}$=7 cm. from the glass (not from the eye).

E. Review of Illustrative Cases ‡

Case 4.—A lawyer, age 39. O.D. allegedly "blind" since 1926 because of retinal detachment. O.S., retinal detachment since 1936, operated on several times.

O.D.: extensive degeneration of the retina, with pigment formation, except in the superior nasal quadrant. O.S.: total retinal detachment. O.D.: vision 20/300 (RV=15) in a small eccentric remnant of the field inferotemporally. O.S.: only light perception.

July 6, 1947: A +33 D. lens was prescribed for the right eye, for exercise. A linen tester of this strength was attached to a spectacle frame.

July 6, 1948: O.D. showed 20/300 vision, but Jaeger 5 could be read with a +20 D. lens.

May 11, 1950: He had learned to read so well with this glass that he had resumed his activities as a lawyer successfully.

Case 5.—Age 12. O.D.: complicated cataract, zonular keratitis. O.S.: secondary cataract after operation, zonular keratitis. O.D.: poor light projection. O.S.: vision 1/60; with +40 D. Jaeger 9. Two discissions were performed on the left eye, on Nov. 5, 1946, and Feb. 12, 1947.

May 31, 1947: O.S.: +12 D. 10/200; +40 D. Jg 1.

April 17, 1952: +12 D. 20/200; +22 D. Jg 5.

Case 6.—Age 71. Sept. 14, 1953: Patient had not been able to read for one and a half years. O.D.: anophthalmos. O.S.: atypical Kuhnt-Junius macular degeneration. O.D.: +1.25 D. 20/300 (RV=15). With +30 D. he read Jaeger 7 at about 3 cm. (corresponding with an RV of $\frac{140}{3}$=46); +30 D. was prescribed.

Oct. 26, 1953: He read Jaeger 5 with +30 D. (corresponding with an RV of 30).

March 27, 1954: He read an ordinary book with +30 D.

Note—Here the "near vision" was poorer than the "far vision" because of a "partial" destruction of the macula (See Sect. B III).

Case 7.—Age 24, 1940. Partial optic atrophy following retrobulbar neuritis O.U. Central scotoma O.U.: O.D. 1/48; O.S. 1/40. With a microglass of +50 D. (linen tester attached to a spectacle frame) on the left eye, the patient could read ordinary print. Later, it was learned that he was able to resume and complete his studies.

Case 8.—Age 28. Feb. 6, 1952: multiple sclerosis (?). Sudden blurring of vision in 1942; O.D. worse than O.S. In both eyes, severe pallor of the disc, temporally more than nasally. Severe asymmetric gaze nystagmus, to the right more than to the left. Large central and paracentral scotomas.

O.D.: 20/150 (RV=7.5); with +10 D. Jg 6. O.S. 20/400; with +10 D. Jg 11. A correction of +10 D. was prescribed for the right eye.

Oct. 23, 1954: O.D. read Jaeger 5 with +10 D. at about 10 cm. (but also some short words of Jaeger 1). He could read a book, could work, and was satisfied with his near vision.

Case 9.—Age 49. Jan. 18, 1944: Primary syphilitic optic atrophy O.U. O.D.: light perception. O.S.: 20/300 (RV=15); visual field severely constricted. O.S.: With +20 D. Jaeger 4 with difficulty.

March 27, 1944: O.S.: With +20 D. Jaeger 3.

Case 10.—Age 56. June 14, 1943: diabetic retinopathy with hemorrhages into the vitreous.

‡ The far vision was often tested at a shorter distance (10-11 ft.) and converted to a distance of 20 ft.

O.D.: light perception; O.S.: 1/24 (RV=24). Lens of +15 D. was prescribed for reading headlines.

Aug. 27, 1943: Vision in the left eye had improved to 20/80 (RV=4). With +8 D., the patient read Jaeger 1.

Dec. 10, 1943: O.S.: 20/80; +4.5 D. was now prescribed for reading (Jaeger 2).

May 20, 1946: O.S.: 20/70; with +4.5 D. Jaeger 1.

May 2, 1949: Last examination; vision 20/60.

CASE 11.—Severe temporal pallor, following retrobulbar neuritis O.U. Severe nystagmus in right and left gaze (probably multiple sclerosis). Central scotoma O.U. Vision O.D. 10/200 (RV=20); with +20 D. (30 mm. diameter) patient read Jaeger 5 at 5 cm.

CASE 12.—Age 56. O.S.: anophthalmos; O.D.: glaucoma operation in 1942, cataract extraction April 6, 1954. Field of vision very much constricted, nasally close to center. O.D.: +3.50sph⊃+8.00cyl, ax 60=20/300; +20.00sph.⊃+8.00cyl, ax 60=Jg. 5.

Oct. 13, 1954: O.D.: +17sph⊃+8.00cyl, ax 65=20/120 with difficulty; +14.00sph⊃+8.00cyl, ax 60=Jg. 5.

April 20, 1955: Patient read books with her reading glass.

CASE 13.—Age 71. May 1, 1944: extensive macular changes with hemorrhages; high blood pressure. O.D.: 20/300. O.S,: 20/150, later 20/120 (RV=6). O.S.: +15 D. Jg. 3; +15 D. was prescribed for the left eye.

May 24, 1944:+15 D. Jg. 2.

Nov. 22, 1944: O.D. 20/300; O.S. 20/120. Patient reported she had already read 340 book pages.

Nov. 29, 1945: +11 D. prescribed for reading.

Oct. 16, 1948: O.D. 20/300; O.S. 20/100. This was the last visit before the patient died.

CASE 14.—March 31, 1941: Severe central chorioretinitis O.U. O.D.: With correction vision about 20/600; O.S., about 20/400. Improvement after treatment with injections of tuberculin.

June 21, 1941: O.D. with −2.00sph⊃−4.00cyl, ax 40=20/500; O.S. with −2.00sph⊃−3.50cyl, ax 140=20/300. With added +8 D., patient read newspaper print.

June 27, 1944: O.D. 20/120; O.S. 20/100; with added +8.50 D. Jaeger 1.

Jan. 7, 1947: O.D. 20/150; O.S. 20/70. With added +5 D., the left eye read some words of Jaeger 1 with difficulty.

CASE 15.—Primary syphilitic optic atrophy O.U. O.D. 1/15; O.S. 1/60. Patient could read with a loupe of +13 D.

CASE 16.—Age 24. Sept. 11, 1946: Primary syphilitic optic atrophy. Convergent strabismus O.S.

O.S. blind; O.D. 1/20. With +33 D. (linen tester), patient was able to read Jaeger 5.

CASE 17.—Age 47. Aug. 27, 1953: Atypical Kuhnt-Junius macular degeneration. O.D.: +2.25 D.=20/300; O.S.: +1.75 D.=20/150. He had as reading glasses O.D. +14 D., O.S. +24 D. (Feinbloom). O.S. with +20 D. read Jaeger 5, but also single letters of Jaeger 2; +20 D. was prescribed.

March 16, 1955: O.S.: with +12 D. read Jaeger 4 with difficulty; with +20 D., single letters of Jaeger 1.

CASE 18.—Age 16. June 14, 1940: atypical pigmentary degeneration of the retina with macular foci; large central scotomas. O.D. 1/18; O.S. 1/12. With +20 D. he read Jaeger 4 with difficulty; with +30 D. he read Jaeger 1; +30 D. was prescribed.

July 15, 1940: He read very well with +20 D.

CASE 19.—Age 58. Feb. 23, 1954: severe myopia O.U.; O.D. nuclear sclerosis. O.S. incipient cataract; O.D.: −24 D.=20/100; O.S. −30 D.=20/300; O.D. −12 D. Jg. 1 at 5 cm.; O.S. −16 D. Jg 2 at 7 cm.

CASE 20.—Age 62. Jan. 16, 1954: (consultation) O.D.: operation for retinal detachment in 1938 without success. O.S.: cataract operation eight to nine years ago; four months after operation, retinal detachment, which was operated on six to seven times.

Present findings: O.D.: cataracta complicata; O.S.: With +18.00sph⊃+6.00cyl, ax 170=10/300, with difficulty (RV=15). He had a Feinbloom glass of +20 D.sph⊃+4 D.cyl, ax 170. With this glass, plus a loupe in the form of a tripod, he learned to read typewritten letters.

CASE 21.—Age 37. May 7, 1953: Nicotine amblyopia; centrocoecal scotoma O.U. O.D. 20/300 (RV=15); O.S. 20/400. Since patient still had some accommodation, only +10 D. was

prescribed for reading, but in two forms: (*a*) as a +10 D. magnifying eyeglass; (*b*) as a +10 D. "loupe" (2½×), for seeing in a wider distance.

Case 22.—Age 56. High myopia; extensive central chorioiditis O.U.; incipient cataract O.U. O.D. −25 D.=20/300; O.S. −25 D.=20/300. O.D. without a glass Jaeger 1; O.S. without a glass Jaeger 1 (at 4 cm.). With −11 D. patient read Jaeger 1, with difficulty, at 7 cm.

Case 23.—Age 78. O.D.: old thrombosis of central vein with numerous hemorrhages and, especially, destruction of the macular region; central scotoma. O.D. 1/60; O.S. 20/25; O.D. with +30 D. Jaeger 11. A glass of +20 D. was prescribed for the right eye, for exercise (every day for one-half hour). Later the right eye read Jaeger 11 with +20 D.

Case 24.—Age 57. Aug. 25, 1940: central chorioiditis O.U.; central scotoma O.U. O.D. 10/140; O.S. 10/300. The left eye read ordinary print with +30 D.

In the meantime the number of legally blind persons who were reenabled by microglasses to read common print has increased very much.

Summary

Three reading devices are available: the magnifying eyeglass, the magnifying lens or loupe, and the telescopic loupe.

The "near vision" of an eye, measured with a reading chart, and the "far vision," measured with Snellen's chart (after correction), were found to correspond in general, except for five conditions: Near vision is better than far vision in peripheral opacities of the cornea or of the lens, in irregular astigmatism, and in some cases of nystagmus; near vision is poorer than far vision in central opacities of the cornea or of the lens and with an incomplete central scotoma.

In case of central opacities, near vision may be improved by mydriatics eucatropine [Euphthalmine] and phenylephrine [Neo-Synephrine].

Only with an incomplete central scotoma is the reading glass, as it is computed from the far vision, too weak; it must be increased (50% and more).

The computation is facilitated by the concept of the "reciprocal of vision," or RV; for 20/100 the RV=5. Counting fingers (F. C..) at *n* feet may be described as $\frac{n}{200}$; for F.C. at 10 ft., or $\frac{10}{200}$, the RV=20.

The quotient of 100 divided by the "maximal distance" at which a certain text can be read by a standard eye (20/20) may be called the "characteristic factor" of this text size. The characteristic factors for Jaeger 1, Jaeger 3, and Jaeger 5 are 2.8, 1.4, and 1, respectively. To determine the number of diopters that must be added to the distance glass, the RV of the eye is multiplied by the "factor" characteristic for the intended text size. The amount of available accommodation must be subtracted.

Jaeger 3 corresponds, more or less, with the letters in telephone books; Jaeger 5, with usual typewritten letters. For Jaeger 3, RV has to be multiplied by the factor 1.4.

In severe amblyopia only reading Jaeger 5 is required. Since the factor for Jaeger 5 is 1, the calculation is simple. The number of diopters required equals the reciprocal of the far vision; $D=RV$ (except in some cases of incomplete central scotoma). An RV of 20 (20/400), for example, requires +20 D. Magnifying eyeglasses are available up to +50 D. and more. The text must be held at the focal point of the "added" lens, i.e., $\frac{100}{RV}$ cm. from the lens.

To avoid the disturbing peripheral aberration, strong glasses with reduced diameter may be used, so-called "microglasses": 30 mm. for +20 D., 20 mm. for +33 D., 12 mm. for +50 D.

Microglasses are now produced in the desired strength and with the desired

diameter. In severe cases it may be useful to use a commercial linen tester attached to a spectacles frame for temporary exercise. The principle of the magnifying eyeglass described is recently used in other forms (two planoconvex lenses of half the strength superimposed on each other, and compound lenses). Microglasses, as well as the other forms, should be determined on the basis of the formula $D=RV$, not by trial and error

Usually the patient is immediately able to read, but sometimes with some difficulty. Exercise improves the reading ability.

A strong loupe gives the maximal magnification if the object lies in its focal plane ("focal position" of the object). Loupes are usually not calibrated in diopters, but are designated by their "real magnification" in the focal position of the object. The real magnification is $\frac{D}{4}$ and is independent of the distance between eye and lens.

In low degrees of amblyopia, down to 20/50, a slightly increased plus glass is "added" for reading. In moderate amblyopia (20/60-20/200), one has the choice of three devices, magnifying eyeglass, loupe, and telescopic loupe, and must consider whether smaller print at a closer distance or a larger print at a greater distance is more important in the individual case. The strength of the required magnifying eyeglass equals RV for Jaeger 5; it equals RV×1.4 for Jaeger 3. The required "magnification" of a loupe is $\frac{RV}{4}$ for Jaeger 5, and is $\frac{RV}{4}\times 1.4=\frac{RV}{3}$ for Jaeger 3.

In severe amblyopia (20/300-4/200) a loupe cannot be used because the field visualized through the lens is too small; neither is an adequate telescopic loupe available. A magnifying eyeglass can be used up to +50 D. and more in the form of a microglass or some other device, so that even with vision of F. C. at 4 ft., as in complete defect of the macula, typewritten letters can be read.

A series of patients who had not been able to read for a long time and were reenabled by this technique to read typewritten texts is briefly reviewed. The number of such patients increased very much in the meantime.

It belongs to the most elating experiences that a half-blind person gets a glass found by computation and is immediately able to read common print.

Appendix

1. Magnification by a Loupe (Fig. 4)

The term angular magnification may be used for the ratio between the visual angle in which an object appears, with and without the loupe.

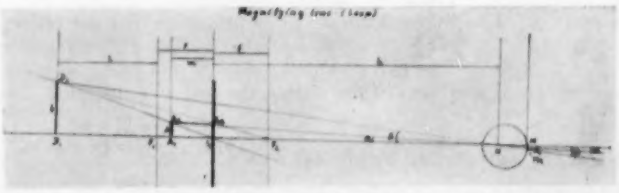

Fig. 4.—Angular magnification of a magnifying lens. L indicates thin lens; F_1 and F_2, focal points of the lens; a, A_1A_2, object; b, B_1B_2, image due to the lens; N, consolidated points of the eye; M, center of the macula; MM_1, image of the object on the retina without the loupe; MM_2, image of b on the retina; f, principal focal distance of the lens; m, A_1L_2, object-lens distance; h, lens-eye (nodal point) distance; t, $m+h$, object-eye distance; l, BF, image-focal point distance. Angle α, M_1NM; angle β, M_2NM. M_a equals angular magnification of the lens.

(*a*) *Angular Magnification* [M_a] *by a Magnifying Lens* (Loupe).—The following formulas are derived

$$M_a=\frac{M_2M}{M_1M}=\frac{tg\beta}{tg\alpha}=\frac{B_1B_2\times A_1N}{B_1N}=\frac{b}{a}\times\frac{m+h}{l+f+h} \quad (1)$$

$$\frac{b}{a}=\frac{l+f}{m} \quad (2)$$

$$\frac{b}{L_1L_2}=\frac{B_1F_2}{L_1F_2};L_1L_2=a;\frac{b}{a}=\frac{l+2f}{f} \quad (3)$$

Hence

$$bf=al+2af$$

$$bm=al+af$$

$$b\times(f-m)=af;\frac{b}{a}=\frac{f}{f-m} \quad (4)$$

From (2) and (3) there follows:

$$\frac{l+f}{m}=\frac{l+2f}{f};lf+f^2=lm+2fm\ ;\ l=\frac{2fm-f^2}{f-m} \quad (5)$$

From (1), (4), and (5) there follows:

$$M_a=\frac{f}{f-m}\times\frac{m+h}{\frac{2fm-f^2}{f-m}+f+h}=\frac{f(m+h)\times(f-m)}{(f-m)\times(2fm-f^2+f^2-fm+fh-hm)}=\frac{f(m+h)}{f(m+h)-hm} \quad (6)$$

or, since $m+h=t$, $M_a=\frac{ft}{ft+(t-m)\times m}$ (6a)

Consideration of the Formula (6): M_a increases if the product $h.m$ increases. The product $h.m$ is maximum if $h=m$, that is, if the lens lies in the midposition between object and eye. Such a position, however, is optically unavailable for strong lenses, where f, the focal distance, would then be less than half the object-eye distance.

If the object-lens distance is greater than the focal distance of the lens, the light rays originating from the object are not parallel, but convergent after passing through the lens, and hence cannot be united on the retina of an emmetropic eye.§ Therefore practically the highest magnification of a strong lens is achieved if the object lies in the focal plane of the lens ("focal position" of the object).

If the object lies in the focal plane, if $m=f$, the Equation (6a) changes, as follows:

$$M_a=\frac{f\times t}{f\times t-f(t-f)}=\frac{t}{f} \quad (7)$$

The angular magnification increases with the object-eye distance and decreases with the focal distance of the lens.

(*b*) *Real Magnification by the Loupe* (M_r).—One must also consider that the original size of the object, if measured in angle degrees, varies inversely with the object-eye distance. Conventionally, an object-eye distance of 25 cm. has been accepted as the standard distance for near vision (von Rohr[3]). An object which measures n degrees at 25 cm. distance will measure $n.\frac{25}{t}$ degrees when it lies at t cm. The magnification (or minification) of the object due to its position $M_p=\frac{25}{t}$. (8)

Therefore, in "focal position" of the object, the real magnification

$$M_r=M_a\times M_p=\frac{t}{f}\times\frac{25}{t}=\frac{25}{f} \quad (9)$$

Since for a lens, surrounded by air, $1D.=\frac{100}{f}$, $M_r=\frac{D}{4}$ (9a)

RULE.—The real magnification of a lens equals one-fourth its power measured in diopters (in "focal position" of the object).‖

§ This would, of course, be achieved by placing a minus glass in front of the eye. Such a combination of a plus glass as "objective" and a minus glass as "ocular" constitutes a telescopic system.

‖ Weak lenses are also used in "subfocal position of the object."

2. Required Position of Reading Text in Use of a Magnifying Eyeglass

If an eyeglass of +20 D. is used, then $f=5$ cm., and the lens-eye distance, $h,=2$ cm., approximately. If the object lies 5 cm. from the eyeglass, i.e., in its focal plane, $m=5$ cm.

According to the Equation (6), $M_a=\frac{f(m+h)}{f(m+h)-h\times m}=\frac{5\times(5+2)}{5\times(5+2)-10}=\frac{35}{25}$

According to the Equation (8), $M_p=\frac{25}{f}=\frac{25}{m+h}=\frac{25}{7}$

Hence, the real magnification $M_r=\frac{35}{25}\times\frac{25}{7}$ is $5\times$.

If the object lies 5 cm. from the nodal point of the eye, i.e., 3 cm. from the eyeglass

$M_a=\frac{5\times(3+2)}{5\times(3+2)-6}=\frac{25}{19}$; $M_p=\frac{25}{5}$, and $M_r=\frac{25}{19}\times\frac{25}{5}=6.6\times$.

3. "Field," as Limited by Margin of Lens

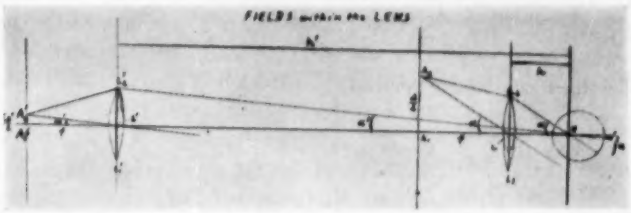

Fig. 5.—Restriction of the "field" by a micro-glass and by a loupe.

$A_2L'''L_2N$; $A_1L=f$; $LL_2=r$ (radius of the lens); $LN=h$ (lens-eye distance)

$A_2'L'''L_2'N$; $A_1'L'=f$; $L'L_2'=r$ (radius of the lens); $L'N=h'$ (lens-eye distance)

A_1A_2 and $A_1'A_2'$ are halves of the diameters of the "fields" (d and d'), respectively

$A_1A_2=f\times tg_a$; $tg_a=\frac{LL_2}{LN}=\frac{r}{h}$; $A_1A_2=\frac{f\times r}{h}$; $d=\frac{f\times r\times 2}{h}$

$A_1'A_2'=f\times tg_a'$; $tg_a'=\frac{L'L_2'}{L'N}=\frac{r}{h'}$; $A_1'A_2'=\frac{f\times r}{h'}$; $d'=\frac{f\times r\times 2}{h'}$

Hence the "field," limited by the margin of the lens, is inversely proportional to the distance between lens and eye.

If the average size of a typewritten letter is assumed to be approximately 0.25 cm., the number of letters visualized within the entire diameter is

$$4d=4\times 2\times\frac{f\times r}{h}=8\frac{f\times r}{h}\text{ or }8\frac{f\times r}{h_1},$$

respectively.

For example, if used as an eyeglass at 2 cm. from the nodal point of the eye ($h=2$ cm.), a lens of +50 D. ($f=2$ cm.) with a diameter of 12 mm. (radius=0.6 cm.) allows one to see $\frac{8\times 2\times 0.6}{2}$, or 4.8 letters. If the same lens is used as a loupe at 20 cm. from the eye, only 0.48 letter, i.e., less than half a letter, can be seen.

For an eyeglass ($h=2$ cm.) of +33 D. ($f=3$ cm.) with a diameter of 20 mm. (radius=1 cm.), the number of visualized letters is $\frac{8.f.r.}{h}=\frac{8.3.1.}{2}=12$.

4. Magnification by a Telescopic System (Fig. 6)

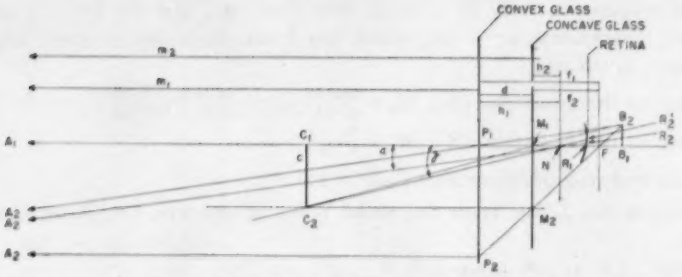

Fig. 6.—Magnification by a telescopic system. $A_1A_2=a$ indicates object; $B_1B_2=b$, image due to the plus lens; $C_1C_2=c$, image due to the system; R_1R_2, retinal image of a; R_1R_2', retinal image of c. $NP_1=h_1$; $NM_1=h_2$ (distances between the lenses and the eye's nodal point). $AP_1=m_1$; $AM_1=m_2$ (distances between the object and the lenses). $FP_1=f_1$; $FM_1=f_2$ (focal distances of the two lenses). $d=h_1-h_2=f_1-f_2=m_2-m_1$ (distance between the two lenses).

The following formulas are derived:

M=magnification due to the entire system

$M=\frac{R_1R_2'}{R_1R_2}$; $R_1R_2'=\frac{NR_1\times C_1C_2}{C_1N}$; $R_1R_2=\frac{NR_1\times A_1A_2}{A_1N}$

$M=\frac{NR_1\times C_1C_2\times A_1N}{C_1N\times NR_1\times A_1A_2}$ Since $A_1N=h_1+m_1$, $A_1A_2=a$, *and* $C_1C_2=c$

$$M=\frac{c(h_1+m_1)}{C_1N\times a} \tag{1}$$

$$c=C_1C_2=M_1M_2;M_1M_2:P_1P_2=f_2:f_1;P_1P_2=A_1A_2=a \text{ ;hence } c=\frac{a\times f_2}{f_1} \tag{2}$$

$C_1N=C_1M_1+h_2;C_1M_1:C_1C_2=B_1M_1:B_1B_2$; $C_1M_1=\frac{c\times B_1M_1}{B_1B_2}=\frac{a\times f_2}{f_1}\times\frac{B_1M_1}{b}=\frac{a}{b}\times\frac{f_2}{f_1}\times B_1M_1$

$a:b=A_1P_1:B_1P_1$

Since $A_1P_1=m_1$

$$\frac{a}{b}=\frac{m_1}{B_1P_1};C_1M_1=\frac{m_1}{B_1P}\times\frac{f_2}{f_1}\times B_1M_1 \tag{3}$$

$C_1N=h_2+\frac{m_1}{B_1P}\times\frac{f_2}{f_1}\times B_1M_1=\frac{h_2\times f_1\times B_1P_1+f_2\times m_1\times B_1M_1}{f_1\times B_1P_1}$;

From (1), (2), and (3) it follows:

$$M=\frac{a\times f_2\times(h_1+m_1)\times f_1\times B_1P_1}{f_1\times a\times(h_2f_1\times B_1P_1\times f_2m_1\times B_1M_1)}=\frac{f_2\times(h_1+m_1)\times B_1P_1}{h_2f_1\times B_1P_1+f_2m_1\times B_1M_1}=\frac{f_2h_1\times B_1P_1+f_2m_1\times B_1P_1}{f_1h_2\times B_1P_1+f_2m_1\times B_1M_1}$$

If the object is very distant, so that f_1,f_2,h_1,h_2, A_1 B_1M_1, and B_1P_1 are very small, if compared with m_1, *the products* f_2h_1 .$\times B_1P_1$, *and* $f_1h_2\times B_1P_1$ may be neglected and $\frac{B_1P_1}{B_1M_1}$ approaches $\frac{FP_1}{FM_1}=\frac{f_1}{f_2}$, so that

$$M=\frac{f_2m_1\times B_1P_1}{f_2m_1\times B_1M_1}=\frac{B_1P_1}{B_1M_1}=\frac{FP_1}{FM_1}=\frac{f_1}{f_2}$$

or, expressed in diopters, $M=\frac{D_1}{D_2}$.

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International Council of Ophthalmology

(Special Report)

STEWART DUKE-ELDER, M.D., London

The following is a résumé of the Minutes of the annual meeting held in Paris on May 5, 1956. Present: Duke-Elder (President), Berens (Vice-President), Hartmann (Secretary), Amsler (Treasurer). Ex-officio: Bietti (President, International Organization Against Trachoma), Coppez (President, International Congress, Brussels), Franceschetti (President, International Association for the Prevention of Blindness), Payne (President, Pan-American Ophthalmological Society), Alvaro (Brazil), Arruga (Spain), Charamis (Greece), Lyle (Great Britan), Marshall (Canada), Paufique (France), Thiel (Germany), Weve (Holland). By invitation: François (Secretary, International Congress, Brussels), Copper (Editor, Index Ophthalmologicus).

Routine reports were made by the President and the Treasurer dealing with the general position and the affairs of the Council during the previous year.

International Dictionary of Ophthalmological Terms

It was reported that the authors of the various languages (Alvaro, Arruga [Spanish], Amsler [French, German], Bietti [Italian, Latin], and Duke-Elder [English]) had completed their work and that the manuscript of the Dictionary was now in the hands of the printers.

Index Ophthalmologicus

Arrangements were made for the publication of the "Index Ophthalmologicus" (the world directory of ophthalmologists, ophthalmic hospitals, etc.) at the International Congress in Brussels, in 1958.

XVIII International Congress in Brussels in September, 1958

It was decided that the administrative languages would be English, French, and German and that the ordinary subscription would be 1500 Belgian francs, with an addition of approximately 10% for those attending who are not members of a society affiliated with the Federation and a reduction to approximately 30% for associates or scientific associates. If the *Acta* of the Congress were to retain its previous luxurious form, the subscription to the Congress would have had to be increased; permission was therefore given to the Belgian Organizing Committee to reduce their commitments in printing the *Acta* so that their expenses would be covered by this subscription. The main discussions were chosen to be "The Orthoptic [nonoperative] Treatment of Stabismus," and "Gerontology in Ophthalmology." For the first, the following were to be invited as opening speakers: Lyle, Malbran, and Bangerter; for the second: François, Buerger, and Jayle.

Submitted for publication May 25, 1956.

European Ophthalmological Society

The creation of a European Ophthalmological Society on lines similar to those of the Pan-American Ophthalmological Society was discussed, and it was decided that François (Belgium) and Riise (Norway) would explore the possibilities of creating such a Society and report to the Council at the next meeting.

The Organization of International Congresses

A considerable discussion took place on changes which might be introduced in the organization of future International Congresses, and a subcommittee consisting of Alvaro, Berens, Duke-Elder, and Thiel was appointed to present a report to the next meeting of the Council.

Committees on Road Safety

The committee charged with studying optical problems associated with safety on roads presented an interim report, and an interim report was received from Blum (Geneva) acquainting the Council with the work of the consultant group on medical requirements in the licensing of motor vehicle drivers.

Statutes and Rules

A discussion took place on the statutes of the International Federation, the International Council, and the internal organization of International Congresses; the President and Secretary were asked to prepare a report before these statutes were finally confirmed at the International Congress in 1958.

History of International Ophthalmological Congresses

In view of the fact that the Congress in Brussels nearly marks the centenary of the 1st International Congress, it was suggested that the President prepare a short history of these meetings during the last hundred years.

Next Meeting

The next meeting of the Council will be held in London on April 10, 1957.

Annual Reviews

THE ORBIT

A Review of the Literature for 1955

ALBERT N. LEMOINE Jr., M.D.
Kansas City

SINCE the last review in this field, by A. G. DeVoe,[1] in the ARCHIVES OF OPHTHALMOLOGY, there have been several articles, but most of these are case reports. The review by DeVoe is excellent and contains a complete summary of the literature of 1954 and early 1955, in addition to several articles from 1952 and 1953 that were not available for the previous reviews. This review repeats the early part of 1955, covering the period from January, 1955, to January, 1956.

It is apparent that very little basic research is being done in reference to the orbit. The literature, for the most part, concerns reports of interesting cases and a few new surgical procedures. One can realize that this would be true in view of the lack of tissue lending itself to basic investigation. The general outline of this review will be the same as that used by DeVoe.

Anatomy

An interesting study of optic nerve sheath pathology was made by S. Levine and M. Bornstein,[2] using anatomical and injection studies. The authors demonstrated a continuity between the cranial, subdural, and subarachnoid spaces and the optic nerve spaces. They reported one case of granuloma and one of tumor entering the orbit by these spaces.

A study of the changes in the orbital glands of the rabbit induced by x-ray irradiation was reported by Cogan, Fink, and Donaldson.[3] The authors subjected rabbits to x-ray irradiation of from 1000 to 4000 r, using one orbit as a control. It is interesting that there was a change in the size of the orbital glands but very little histological change.

Diagnostic Methods and Instrumentation

Carroll and deRoeth[4] reported on the effect of retrobulbar procaine on the optic nerve. As one would expect, the more complete the motor block the greater the visual reduction. In some subjects the visual reduction was to nil, but complete recovery of vision was reported within 30 to 120 minutes.

The continued interest in methods of demonstrating orbital lesions by the use of contrast media was reported by Cowie and Groves.[5] In this study air, oil, and water-soluble materials were used. The injections were made within the fascial planes, and x-rays were taken. There were four cases in which the authors believed that disturbances in the fascial planes could be demonstrated by contrast media methods. The injection of 17% iodopyracet (Diodone) into the tissue spaces was best and was followed by minimal adverse effects. The authors feel that the procedure is safe for clinical use.

A unique method for producing constant orbital pressure was reported by McCullock and Cowan.[6] Following surgery of the orbit, when it is desirable to

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have constant pressure, a vinyl plastic bag is placed under a Wheeler patch. The plastic bag is attached to a manometer, and the desired pressure is obtained by inflation of the bag. The advantages claimed are the ability to have a known amount of pressure and to change the pressure without a new bandage. This procedure should be most useful when one is faced with uncontrolled bleeding in the older age group.

Czukrasz [7] reported a series of Kronlein operations. The complications were the same as those previously reported, with good exposure for tumors in the lateral half of the orbit.

The search for the ideal implant following enucleation continues.* Several modifications of shapes and sizes have been reported, but the problem with the integrated implant continues to be extrusion and chronic infection. The importance of preservation of tissue and retention of the superior and inferior fornices continues to be stressed by all of the authors. The trend to the use of completely buried implants continues, with no article encouraging the use of an integrated implant, except for the one by Arruga.[9] The use of some type of intrascleral implant is suggested, but the danger of an unrecognized intraocular tumor or sympathetic ophthalmia cannot be stressed too much when one considers this type of surgical approach.

Seven cases of tantalum orbitopasty were reported by Callahan.[14] The problems related to the insertion of the tantalum plates are reported, but the final results appear to be satisfactory. The danger of the use of such plates in the presence of chronic infection or osteomylitis must be considered.

Congenital and Developmental Anomalies

Urrits-Zavalia [15] reported a family with multiple developmental anomalies with dominant inheritance. The anomalies vary from one member to the other, with changes involving one or both orbits, tissues of the lids, and the lacrimal apparatus.

Zinn [16] reported a single case of cryptophthalmia. This unusual defect presents serious problems in the management of the patient from the point of view of both the cosmetic and the functional abnormality.

Hope and co-workers [17] reported on the importance of early recognition of premature cranial synostosis. The importance of the shallow orbit and prominent eyes as an aid to early recognition should be realized by the ophthalmologist. The fact that the brain undergoes 80% of its growth within the first three years of life is important in early diagnosis.

Extreme bilateral orbital cysts occurring in a Bantu infant were reported by Skapinker.[18] The cause of the cysts was not determined, but after surgical removal there was a good recovery. The cysts produced a profound degree of bilateral exophthalmos and marked divergence.

Inflammation

A child with mucormycosis who recovered was reported by Harris.[19] This is a most interesting case report because the diagnosis was not made at autopsy. Treatment was with oxytetracycline (Terramycin), iodides, penicillin, and a vaccine made from cultures grown from the orbit. The child was diabetic and poorly controlled. The development of a rapidly progressing orbital or nasal

* References 8-13.

infection in a child with diabetes or chronic illness should suggest the possibility of this type of infection.

Three cases of acute nonspecific infection of the orbit were reported by Kerkenezor.[20] The etiology of the orbital cellulitis was not determined.

Relation of Paranasal Sinuses and Teeth to Ocular Disease

Dawes and Levene[21] reported a case of acute myeloid leukemia with the presenting symptoms of acute frontal sinusitis. There was a rapidly developing septicemia with death. The importance of a blood examination in patients with orbital cellulitis is apparent in this case report.

Bilateral exophthalmos in a case of rhabdomyosarcoma of the nasopharynx was reported by St. John and Woo.[22] There was complete extrusion of the orbital contents on one side as the result of the tumor growth. X-ray therapy caused some regression of the tumor mass and a reduction of the exophthalmos but did not prevent death.

Three cases of malignant granuloma of the orbit treated with cortisone and x-ray were reported by Howells.[23] The process was extremely destructive to orbital tissue, but all three patients survived.

A fatal case of carcinoma of the maxillary sinus in a youth of 20 years was reported by McMahon.[24] The presenting complaint was unilateral exophthalmos, with death occurring within two months from intracranial extension despite radical therapy.

Neuroblastoma arising from the nasal fossa was reported by Fisher.[25] The tumor was of an undifferentiated type removed by local excision. Death resulted from metastatic lesions to the lung and brain.

Skolnik and Fornatto[26] reported the apparent cure of four patients with ossifying fibromas of the paranasal sinuses. The difficulty of making a diagnosis is due to minimal x-ray changes and the slow growth. Complete surgical removal is advised.

Injuries

An interesting report of the use of laminagraphy in acute maxillofacial injuries was made by McClure.[27] The author was able to demonstrate fractures of the bones of the orbit by this method when the usual x-ray studies were negative. This report is encouraging because early diagnosis of fractures in the orbital region may prevent the dreaded late complications of this type of injury.

The early treatment of fractures of the zygoma and orbital floor was reviewed by Rubin.[28] The importance of early elevation of orbital floor fractures may prevent serious muscle palsies and enophthalmos following this type of injury. The author reported on four cases with early treatment and good results.

Doggart's[29] article on the impact of boxing upon the visual apparatus is timely. The orbital changes noted in boxers were diffuse thickening of the bones of the orbital rim, localized hyperosteosis, and fractures of the bones about the orbit. One cannot deny that numerous injuries to the visual apparatus occur in boxing.

Vascular Conditions

The free anastmosis of the vessels of the head and their significance in diagnosing internal carotid artery occlusion was reported by Lin and Scott.[30] In making a diagnosis of internal carotid artery occlusion or thrombosis by angi-

ography one must rule out other cerebral lesions by air studies unless the internal carotid occlusion can be verified by operation or by evidence of collateral circulation, either through the opposite carotid or vertebral artery or by way of the external carotid through the ophthalmic artery, middle meningeal, or muscular branches.

Nonpulsating unilateral exophthalmos due to caroticocavernous fistula was reported by Clarke and co-workers.[31] The authors pointed out that between 10% and 15% of the patients with exophthalmos due to caroticocavernous fistula will not have pulsation. The successful treatment of a case of carotid cavernous fistula by a two-stage neurosurgical clip procedure was reported by Abrahamson and Bell.[32]

Two cases of orbital hematoma were reported by Roberts,[33] and one case of hemangioma was reported by Santayat.[34]

Manifestation of General Disease

Umlauf [35] reported a case of multiple reticuloendothelial granuloma of the skull in which the presenting lesion was on the brow. The characteristic punched-out bone defects of the skull are of diagnostic importance.

Exophthalmos of Thyroid Disease

The problem of etiology and therapy of exophthalmos associated with thyroid disease continues to be confused. Fewer articles than usual on this subject were found in the literature of 1955.†

Smelser and Ozanics [36] reported on further studies on the nature of the exophthalmos-producing principles in pituitary extracts. In their studies corticotropin (ACTH) acting through the adrenals and adrenal steroids augment the exophthalmos produced in guinea pigs by anterior pituitary extracts.

The conclusion of a British committee on the influence of cortisone in thyroid exophthalmos [37] was that there was little if any benefit. This is still a controversial subject, but it appears that the first encouraging reports are now subject to doubt.

Naffziger [38] reported on 40 successive cases of exophthalmos treated by radical surgery. These were patients with malignant exophthalmos (14 males). In five patients there had been neither a thyroidectomy nor recognizable thyroid disturbance. In general, the author's surgical results were satisfactory, with an average reduction of the exophthalmos of 4 to 5 mm.

Albeaux-Fernet and co-workers [39] reported the case of a patient with malignant edematous exophthalmos treated by surgical hypophysectomy. Apparently this patient had a fulminatory course of bilateral exophthalmos that had failed to respond to all the usual forms of medical therapy. After complete removal of the pituitary by surgical curettement there was marked improvement.

In separate articles by Hedges and Scheie [40] and Igersheimer [41] the visual changes in thyroid exophthalmos were reported. Six cases were reported by Hedges and Scheie with central field defects that disappeared after therapy. Igersheimer also reported six cases.

Tumors

Thirty-four cases of children with ossifying fibromas of the facial bones were reported by Georgiade and co-workers.[42] The etiology of this condition is un-

† References 36-42.

known, but surgical removal of the lesions produced satisfactory results.

Donahue [43] reported a most interesting case of a recurrence of an optic nerve glioma 22 years after the initial removal. Despite this long history there was no evidence of involvement of the chiasm.

Love and co-workers [44] reported on the successful treatment by the transfrontal approach of four patients with gliomas affecting the optic nerve. The authors advocate the transfrontal removal of gliomas of the optic nerve rather than an anterior surgical approach.

A case report of meningioma infiltrating the nasal cavity, nasal sinuses, and orbit was made by Belal.[45] The patient died as a result of destruction of the frontal lobe.

It is interesting that two cases of hemangiopericytoma of the orbit were reported in 1955. These are believed to be the first cases of this tumor involving the orbit. The reported cases are by Goodman [46] and Fox.[47] In both patients there was unilateral exophthalmos, with the diagnosis established by surgical removal of tissue.

A patient with plasmocytoma of the orbit treated with x-ray and surgery was reported by Jim.[48]

Clarke [49] wrote a good summary of the ocular complications of multiple myelomatosis. The report concerns all of the ocular structures, including the orbit. A single case report of unilateral exophthalmos due to multiple myelomatosis with proptosis was made by Handousa.[50]

Deering [51] reported a case of basosquamous-cell carcinoma of the orbit requiring exenteration. The primary site apparently was an old skin lesion adjacent to the orbit.

There was a very good review of the diagnosis and treatment of orbital tumors by Foster.[52] This was a general review of the entire problem, with emphasis on methods of differential diagnosis and treatment.

4620 J. C. Nichols Pkwy.

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News and Comment

ANNOUNCEMENTS

National Muscular Dystrophy Research Foundation.—A great milestone in the muscular dystrophy field is the announcement of a five-year $250,000 research project sponsored jointly by the University of Texas Medical Branch in Galveston and the National Muscular Dystrophy Research Foundation.

A check for $10,000—down payment on a quarter million dollars worth of hope—was presented to Dr. John B. Truslow, executive director of the Medical Branch, on Monday, May 7.

"It is the hope of the Medical Branch that by setting up the teamwork approach of many departments the cause and cure of the disease can be found here," Dr. Truslow said.

"The field of endeavor," Dr. Mason Guest, consultant for the Medical Branch hospitals, said, "is wide open."

Dr. Guest is chairman of the department of physiology and will lead a committee of nine medical department men in the broadest possible attack against the ignorance which keeps medical science from finding a cure for muscular dystrophy.

Simultaneously, the Medical Branch will set up the first muscular dystrophy clinic in this part of the United States and will admit patients who have the disease.

The Galveston ceremony at which the grant was announced was homecoming for Sallie and Nadine, founders of National Muscular Dystrophy Research Foundation, for it was at the Medical Branch 12 years ago that the seed for the Foundation was planted. There, for the first time, the illness which had plagued them since childhood was diagnosed as muscular dystrophy.

Others present for the announcement included Mrs. H. W. Gardner, national president of the foundation; Dr. Charles T. Stone Sr., professor of the Medical Branch department of internal medicine and chairman of the Foundation medical advisory board, and Mrs. Julia Langford, field director of the Foundation.

Military Ophthalmologists and Military Otolaryngologists Meeting.—The Society of Military Ophthalmologists and the Society of Military Otolaryngologists will hold a joint stag dinner meeting at the time of the annual meeting of the American Academy of Ophthalmology and Otolaryngology in Chicago in October.

Dinner will be served at 6:30 p.m. on Oct. 16, 1956, at the Palmer House. The dinner will be followed by a short business meeting.

All members of the Society of Military Ophthalmologists and the Society of Military Otolaryngologists are invited to attend. Application may be made to either Capt. James A. Stokes (MC), Secretary-Treasurer, Society of Military Ophthalmologists, Eye Clinic, Walter Reed Army Hospital, Washington 12, D. C., or to Major Stanley H. Bear (MC), 3810th U.S.A.F. Hospital, Maxwell Air Force Base, Ala.

PERSONAL

Dr. Mullen.—Carroll R. Mullen, M.D., has been appointed Professor and Head of the Department of Ophthalmology at The Jefferson Medical College of Philadelphia.

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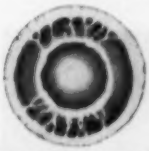

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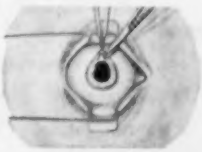

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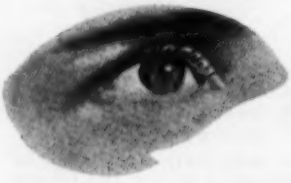

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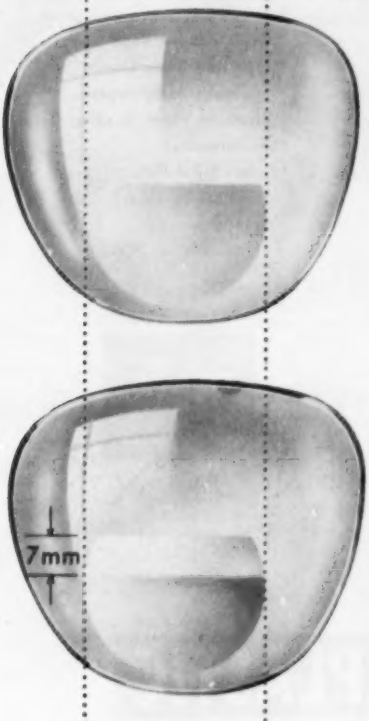

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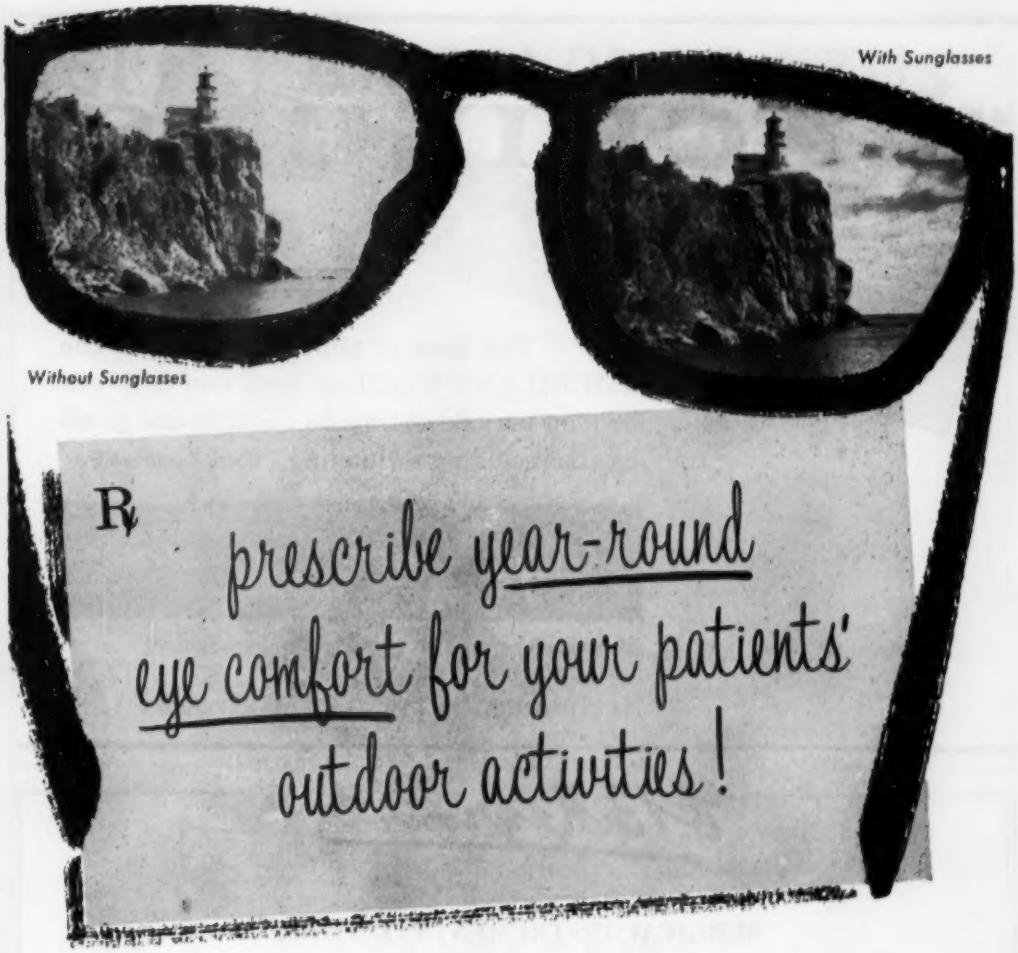

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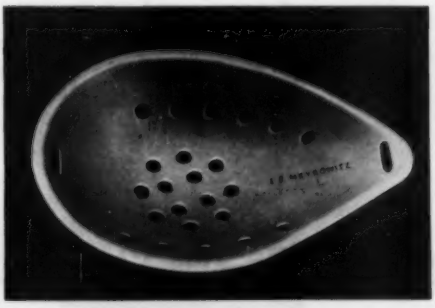

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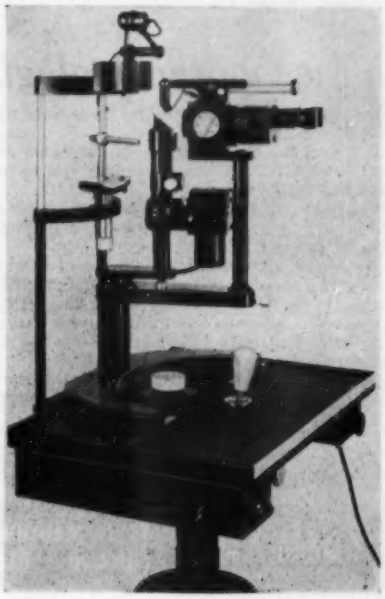

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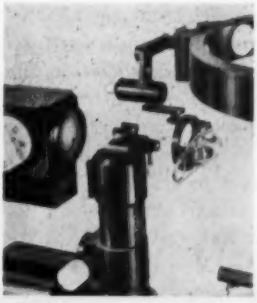

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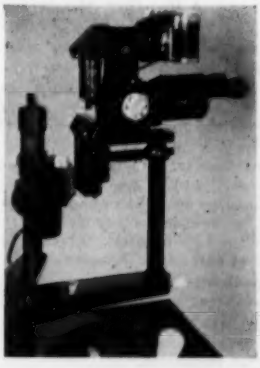

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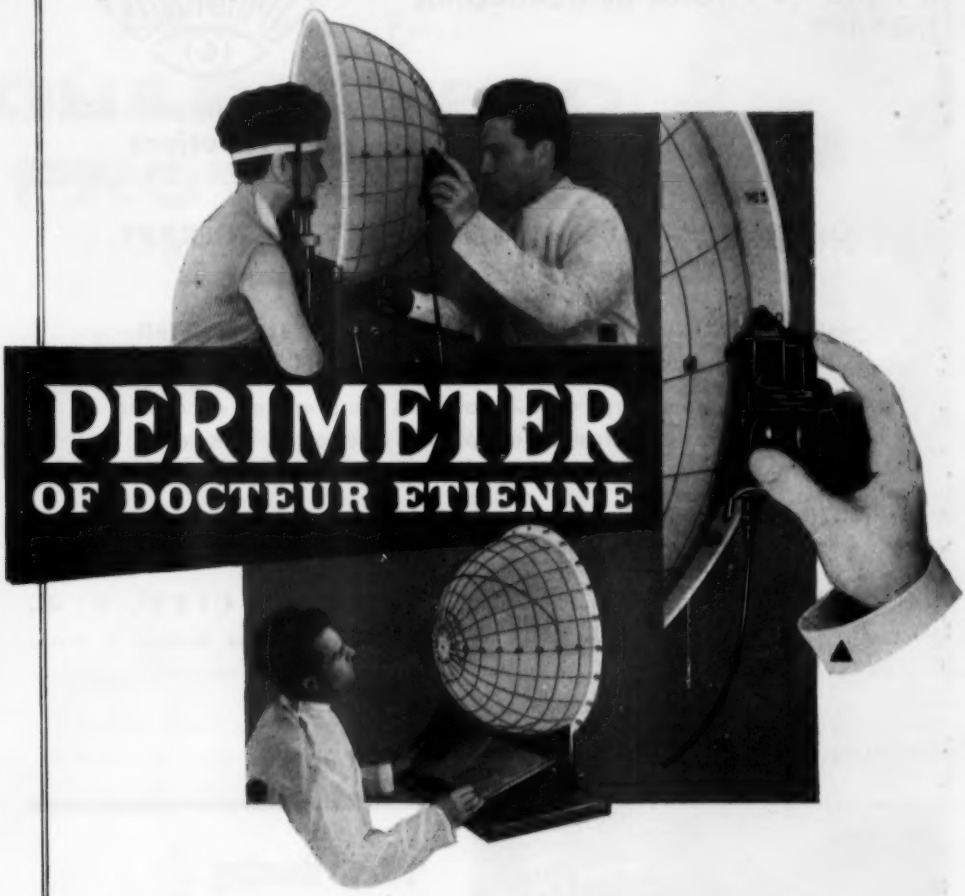

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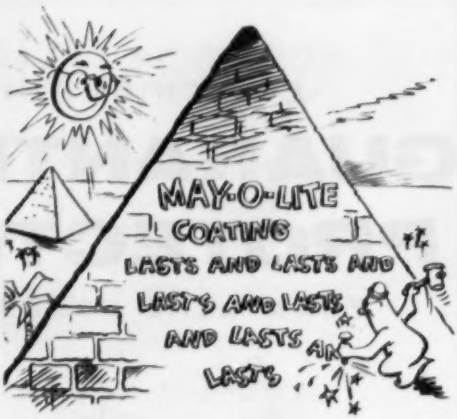

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From the Literature

"... [a] most effective antihypertensive agent..."[1]

"... a simple and [well-tolerated] regimen for the ambulatory management of hypertensive patients."[2]

"... reduction of the blood pressure may be achieved in substantially all forms of hypertension."[3]

"... possible in most patients to get a good control over blood pressure levels with comparatively few side-effects."[4]

"... significant falls ... occurred in systolic and diastolic blood pressure. ... The cardiac, retinal and coronary status of all patients was improved."[5]

1. Moser, M.: New Yor State J. Med. **55**:199 (July 15) 1955. 2. Agres A., and Hoobler, S.W J.A.M.A. **157**:999 (Marc 19) 1955. 3. Smirk, F.H Am. J. Med. **17**:839 (Dec 1954. 4. Smirk, F.H., an McQueen, E.G.: J. Chro Dis. **1**:516 (May) 195 5. Waldman, S., and P ner, L.: Am. J. M. Sc. **231**:14 (Feb.) 1956.

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CASE HISTORY #2

This second case history involving the use of CATAREX T temporary cataract bifocal lenses demonstrates that CATAREX T can be prescribed for and worn to advantage by the patient as early as ten days after cataract surgery.

This advantage is, of course, immeasurably valuable in cases where the patient, by virtue of financial circumstances, must be back on the job as soon as possible.

Catarex Service, when used in conjunction with CATAREX D permanent bifocals, may prove to be useful in *your* practice . . . why not check with your laboratory or optician?

CASE HISTORY – Mrs. X. X.

The patient, a female 68 years of age, was first seen on January 8, 1953, and a diagnosis of right senile cataract was made. The left eye was painful and blind. One week later, an alcohol injection about the left ciliary ganglion relieved the patient of pain and enabled her to retain the eye, which was psychologically most desirable.

On May 18, 1954, a right intracapsular lens extraction was performed without complication. The post-operative course was uneventful and the patient was discharged from the hospital on May 27th. While the patient was still in the hospital, a +10.00D temporary single-vision* lens was ordered and fitted on the patient's first office visit on May 28th. With this lens, the right vision = 20/50.

6-8-54: Manifest O.D. +11.00Dsph. ⊂ +2.50Dcyl. ax 10 = 20/30—. Rx Right: this in CATAREX T (temporary style) straight-top bifocal. Left: lens to balance. The patient was allowed to retain the previous lens until the new CATAREX T bifocal was received. This plan was followed on all subsequent changes.

7-8-54: Manifest O.D. +11.50Dsph. ⊂ +1.50Dcyl. ax 15 = 20/25+. Rx Right: this in CATAREX T. Left: lens to balance.

9-9-54: Manifest O.D. +12.00Dsph. ⊂ +1.25Dcyl. ax 15 = 20/15. Rx Right: this in CATAREX D permanent bifocal. Left: lens to balance.

1-25-56: Sixteen months after securing the permanent CATAREX D bifocal, the Right vision with this lens = 20/15.

This patient, who secured her first CATAREX T (temporary style) lens ten days after cataract surgery and had three different changes, secured her first and only permanent lens approximately four months after surgery. To date, she has not had to have it changed or re-surfaced.

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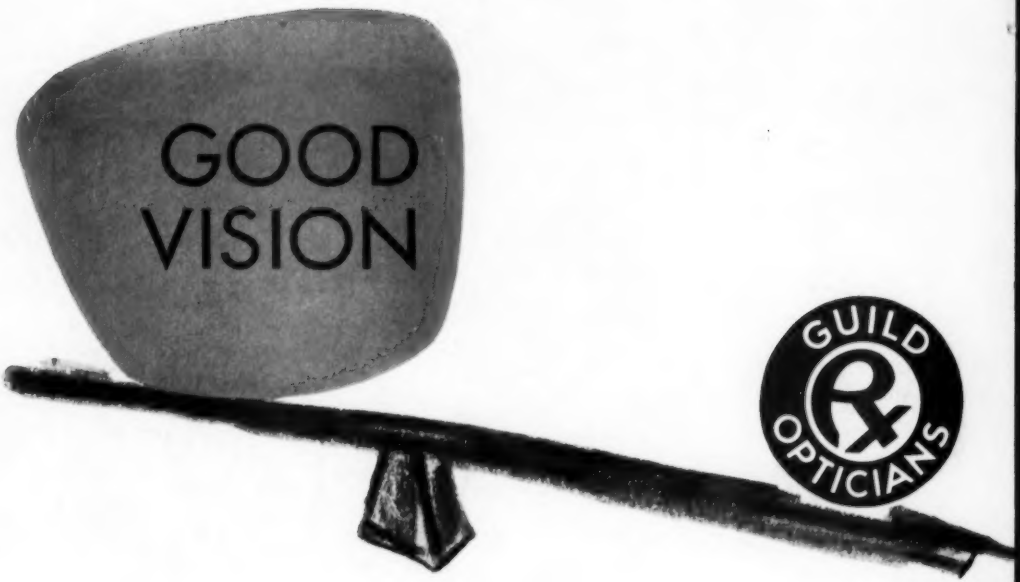

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